Approximating persistence times in stochastic models for infectious disease

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Abstract

We begin with a brief introduction to the history of epidemic models, both deterministic and stochastic, examining existing models and their underlying assumptions. The first model studied is one of the most basic, the SIS model, which can in many cases be considered a special case of the more advanced models. The properties deemed of interest in epidemic studies, such as extinction time, are defined and their features in previously considered work is established.

A number of current approximations to models and the necessary reasons for the approximations are then catalogued, comparing exact results with approximations where available, for the insights that they provide when exact results would require intractable calculations or computational power in excess. Many of the approximations previously studied have been derived as the result of an asymptotic approximation process, and as such may not hold up for finite parameter values or in finite time; this work considers a number of these, and attempts to find practical cases where the appoximatins remain valid.

The focus of the work then shifts to two categories: the creation and derivation of properties of a more complicated and potentially more realistic model, and the approximation of features the existing model by defining parameters.

The primary model considered is that of the SIS-Erlang period, where the SIS model is adapted to contain multiple infectious substages, allowing for the model to better approximate realistic diseases. The model requires a further parameter, but displays different behaviours when contrasted with an SIS model with otherwise identical parameters. Particular focus is given to empirical results of the SIS-Erlang period where the Infectious period has two infectious substages, due to computational complexity. The provided results attempt to parallel previous results from the basic SIS model.

An attempt is then made to create a universal approximation for time to extinction for a limited subset of parameter values, based on previous attempts to determine parameter values for which time to extinction varies monotonically with respect to coefficient of variation. The primary motivation behind the work is that of speed, as the approximation is quickly calcualated, but tradeoffs in accuracy are found to be high in several instances.

Overall, this document attempts to summarise several key points of the basics of the study of epidemic diseases, and assess two previously unconsidered examples in the categories of realistic complications and approximation.

Contents

1 Introduction

Much infectious disease modelling is concerned with studying the initial stages of an epidemic outbreak. A rather different issue is the behaviour of an infection which has become established in the population, i.e. an endemic disease. Quantities of interest include the endemic level of prevalence (proportion of the population infected), and the persistence time (time until the disease eventually dies out). A useful mathematical tool to study these random variables is the quasi-stationary distribution of the process, and a variety of methods exist to approximate this quasi-stationary distribution. This project will investigate the effects of disease features (e.g. distribution of the infectious period) upon disease persistence time, by numerical evaluation of quasi-stationary distributions and analytical study of approximation methods.

The simplest plausible model for endemic infection is the susceptible-infective-susceptible (SIS) model. The time to extinction can be calculated from quasi-stationarity, or from any of the available states. We investigate several existing approximations and derives additional approximations. These are then compared to results for an analogous model with a more realistic infectious period distribution.

Both stochastic and deterministic models are currently frequently used in the study of infectious diseases. Inevitably, any mathematical model which attempts to be accurate to any level of detail will be forced to rely to some degree on probabilistic modelling. When dealing with statistically large numbers of individuals, the influences of fluctuations should be much reduced. In such circumstances, deterministic models can be used well as a first approximation. These models consider the rates of change between classes as time derivatives, and the model is formulated using differential equations, with rates depending on the current numbers of infectives and susceptibles. Much of the early study of epidemiology was deterministic, for as models becomes increasingly complex, it is frequently the case that the deterministic model can remain easier to analyse.

The first study of stochastic models for epidemics began with McKendrick (1926), considering the transmission of disease from one individual to another as being a random event based on the parameters of the disease in question. The study of stochastic models allows us to examine the long term behaviour of a disease, as well as allowing us estimates of the level of uncertainty, neither of which can be found in deterministic models. The resulting probabilities can however frequently become analytically intractable. Various methods of approximation can help allay this somewhat, and help capture the underlying behaviour of the process, in a way that can be useful.

Many stochastic models for the spread of infections diseases predict that eventually, diseases will die out. Expected time to extinction, however, can be very long. The infection may be modelled as a Markov process. The transition rate matrix of such a process can be very large, or in some cases infinite, so approximations such as truncation may be necessary to make calculations tractable. Qualitative insight into the structure of the quasi-stationary distribution is therefore possible. The most common approximation of the quasi-stationary distribution is that of a Gaussian diffusion process, leading to a stationary normal distribution.

In infectious disease modelling a quantity of particular interest is the persistence time until infection dies out of the population. For realistic disease models it is often only possible to study the distribution of this quantity via simulation. For simplified models, some progress can be made analytically.We aim to assess some approximation techniques that have been proposed for the simplest models for endemic infection, with a view to extending such techniques to more realistic models.

Most analytical work in the literature focuses upon asymptotic results in the large population limit. We will instead aim to assess how well each approximation performs for moderate population sizes. We are interested in, firstly, whether a given technique provides a good approximation for the expected persistence time of disease in a finite population; and secondly, whether the technique is generalisable to more realistic models.

Thus we investigate existing methods for approximating time to extinction for the susceptible-infective-susceptible (SIS) model of Weiss and Dishon (1971). We then consider extension to a slightly more realistic model. In modelling infectious disease transmission, it is often assumed that individuals' infectious periods are exponentially distributed. This is a mathematically convenient assumption, equivalent to assuming that the rate of recovery at any instant is constant. In practice, infectious periods have been shown to be less dispersed than the exponential distribution, leading to the existing framework underestimating the number of individuals whose period of infection is significantly larger than the mean, and vice-versa. We will therefore consider an extension to allow the infectious period to follow an Erlang distribution, which is more closely centered about the mean. The impact of Erlang-distributed infectious periods has been investigated by Lloyd (2000) for a susceptible-infective-removed (SIR) model, and by Andersson and Britton (2000) for a susceptible-exposed-infective-removed (SEIR) model. Lloyd (2000) found that for the parameter values of interest, persistence was decreased when comparing an SIR model with its counterpart containing an Erlang-distributed infectious period. Andersson and Britton (2000)

found, inter alia, that time to extinction is increasing with respect to the coefficient of variation of the infectious period.

Even simple stochastic models can be difficult to analyse. Transition rates frequently exhibit non-linear dependence on numbers of individuals, leading to intractable stochastic processes. Techniques of approximation are of vital importance to understand the underlying behaviour of the process. Deterministic approximations are common within the literature, and allow for analysis of many features, but the stochastic process remains the more realistic and powerful approach.

2 Literature review and model formulation

2.1 Early disease modelling

The study of disease models mathematically can be traced back many years, with some of the key principles being recognised early on. For instance Hamer (1906) recognised the dependence of the disease's behaviour on the size of the susceptible population, and the contact rate between susceptibles and infectives. Early stochastic modelling was proposed by McKendrick (1926), who introduced a number of additional features such as variable rates of infection and recovery, culminating in the Threshold Theorem. This theorem states that the introduction of infective individuals into a naive population of susceptibles does not necessarily result in an epidemic outbreak, but only if the density of the susceptibles is high enough.

Many models for diseases have been studied, and some of the most common are the SI (Susceptible-Infective), SIS (Susceptible-Infective-Susceptible) and SIR (Susceptible-Infective-Removed) models. These vary in the structure of the disease, as the ultimate fate of infected individuals changes dynamics greatly. The simple stochastic SIS epidemic model was introduced by Weiss and Dishon (1971), and has since been considered by many other authors, such as Kryscio and Lefèvre (1989), and Nåsell (1999). In this model, infected individuals recover, but gain no immunity from the disease, and may return to being infected. This is mathematically convenient, and may be justified depending on the period of time for which the study is occurring. The SIS model is considered one of the most basic models useful for studying disease behaviour, as it allows for individuals to become re-infected, allowing for long term study of effects on a population. Other models include the SEIS model, where Exposed individuals are added. These are not contagious, and do not affect infection pressures, allowing for some models to adequately represent carriers of a disease.

One of the assumptions made in early disease models, that is still used today, is that the time for which individuals remain infectious can be described adequately by an exponential distribution. This assumption is biologically unreasonable (as are many assumptions, to varying degrees) but very convenient for allowing tractable solutions. This assumption leads to the distribution of infectious periods being too dispersed compared to their realistic state, where they are more closely centred about the mean duration of infection. Some diseases, such as *Chlamydia trachomatis* however, have infectious period length

experimentally fitting an exponential distribution quite well (Rahman et al. 2015).

For some situations, the simplification undertaken is perfectly adequate, however it is less so for others - "Such simplifying assumptions will make little or no difference to some aspects of model behaviour [It can be shown that] there are a number of basic formulae where only the mean of the generation gap or the infectious period is required. Other aspects, however, such as the stability of the endemic conditions, depend sensitively on the distribution of the generation gap" (Mollison 1995).

The value of the simplified models is revealed by adding additional realistic complications to the model, and measuring differences. This is one of the main targets of this thesis, alongside comparisons of existing and new approximation methods. That is, to assess to what extent infectious disease dynamics can meaningfully be approximated by simpler systems.

2.2 SIS epidemic model

We begin by considering one of the most basic models of epidemiology, where infection spreads by contact between members of the community. Members of the population may recover, but do not become immune. Infected individuals are not removed from circulation by death or isolation, and no birth or immigration into the population is permitted. The disease model assumes homogeneous mixing, such that the contact rate between individuals is dependent only on the number of infected and susceptible individuals, as well as a parameter representing the infectiousness of the disease. This is a very popular model, and has been used by many authors since its inception by Weiss and Dishon (1971). Historically, a large number of the analyses of SIS model behaviour have been based on various versions of the forward Kolmogorov differential equations.

In this model, infection spreads between members of a fixed size closed population of size N consisting at time t of $S(t)$ susceptible and $I(t)$ infected individuals. The respective variables take discrete values $I, S \in \{0, 1, 2, ..., N\}$. It is then sufficient to focus on $I(t)$ only, as $S(t) + I(t) = N \ \forall \ t \geq 0$. The process $I(t)$ evolves as a continuous-time Markov chain, with rates of transition as follows.

Event	State transition	Transition rate
Recovery of infected	$I \to I - 1$	γI
Infection of susceptible	$I \to I + 1$	$\frac{\beta}{N} I(N - I)$

Here $\beta, \gamma > 0$ are the infection and recovery rate parameters, respectively. The parameter β represents the infectivity of the disease, whilst $\dfrac{1}{\gamma}$ represents the average period of time taken for any given individual to recover, and return to a state of susceptibility. The basic reproduction number R_0 is defined as the 'average number of new infected individuals that a single infected individual produces in a population of susceptible individuals during the early stages of an epidemic' (Diekmann et al, 1990). In the case of the SIS model this is intuitively given by $R_0 = \beta/\gamma$, as an average infectious individual will remain infectious for $1/\gamma$ period of time, and will produce β infections in a naive population during this time. This number is a key measure of infectivity of a disease, as well as having other uses such as the threshold limit theorem, which states that if and only if $R_0 > 1$ can a major outbreak occur in a large population. In any other situation, the disease will not spread and will eventually die out.

The process has a degenerate stationary distribution at the state $I = 0$; that is, the infection cannot recover from the state when infection is extinct. This is the only absorbing state, all other states being transient. As such, our main focus regards the situation of the process remaining in transient states, which prior to extinction describes the long term behaviour of the process. This is known as the quasi-stationary distribution of the process, and will be discussed later.

2.2.1 Deterministic model

A deterministic process is one whose outcome, and therefore features, can be exactly predicted if given full information of the initial state. When investigating epidemic behaviour, deterministic models are frequently used, such as Kermack and McKendrick (1927). They do provide some differences in analysis, as some phenomena exist purely in stochastic models, such as the probability of a major outbreak. Given a low number of initial infectives, there may exist the distinct possibilities of a large epidemic, and of early extinction, the probabilities of which can only be calculated when considering the model in a stochastic setting.

To formulate a deterministic version of the SIS epidemic model, we first introduce the scaling $s(t) =$

$\frac{S(t)}{N}$ and $i(t) = \frac{I(t)}{N}$, where N is considered sufficiently large for the states to be analysed as continuous variables. While stochastic models describe the spread of a disease as one of chance, in terms of the probability of spreading, deterministic models assume mass action, relying on the law of large numbers. As $s(t) + i(t) = 1$, the equivalent deterministic process can then be completely described in the single equation

$$\frac{di}{dt} = \beta(1-i)i - \gamma i. \tag{1}$$

This system is in equilibrium when

$$i(\beta - \beta i - \gamma) = 0,$$

resulting in equilibria

$$i = 0 \text{ and } i^* = 1 - \frac{\gamma}{\beta}. \tag{2}$$

The first equilibrium represents the disease free state, whilst the latter represents the endemic level. An equilibrium is considered (locally) stable if after any 'disturbance' ϵ the system returns to equilibrium. That is, for an equilibrium point i^*,

$$\left.\frac{di}{dt}\right|_{i^*-\epsilon} > 0 \text{ and } \left.\frac{di}{dt}\right|_{i^*+\epsilon} < 0.$$

The condition for stability is thus

$$\frac{\partial}{\partial i}\left(\frac{di}{dt}\right)\bigg|_{i^*} < 0.$$

At the first equilibirum, $i = 0$, the case of extinction,

$$\frac{\partial}{\partial i}\left(\frac{di}{dt}\right)\bigg|_{i=0} = (\beta(1-2i) - \gamma)\bigg|_{i=0} = \beta - \gamma.$$

That is, the equilibrium is locally stable when $\gamma > \beta$.

Conversely, for the endemic equilibrium,

$$\frac{\partial}{\partial i}\left(\frac{di}{dt}\right)\bigg|_{i^*=1-\frac{\gamma}{\beta}} = (\beta(1-2i) - \gamma)\bigg|_{i^*=1-\frac{\gamma}{\beta}} = \gamma - \beta.$$

That is, the equilibrium is stable when $\beta > \gamma$. It can then be seen that the extinction equilibrium is only stable for values of $R_0 \leq 1$ whilst the endemic equilibrium is only stable for $R_0 > 1$.

2.2.2 Stochastic model

Although in the stochastic model, extinction is assured regardless of the value of R_0, processes for which the time to extinction is large can display an equilibrium distribution of sorts on the non-absorbing states, as discussed in Van Doorn and Schrijner (1995). This can be seen as an analogue to the deterministic endemic equilibrium as shown above. This limiting conditional distribution $\boldsymbol{q}$ is defined by conditioning on the process's non-extinction as time tends to infinity, that is $\boldsymbol{q} = (q_1, q_2, \ldots, q_N)$ where

$$q_i = \lim_{t\to\infty} \mathbb{P}(I(t) = i \mid I(t) > 0) \text{ for } i = 1, 2, \ldots, N.$$

A quasi-stationary distribution is any distribution $\mathbf{q}$ satisfying

$$\mathbb{P}(I(t) = i \mid I(t) > 0, I(0) \sim \boldsymbol{q}) = q_i \text{ for all } t > 0.$$

For a process on a finite state space, with a single absorbing state and other states communicating, there exists a unique quasi-stationary distribution, which is also the unique limiting conditional distribution (Darroch and Seneta, 1967). To practically calculate this quasi-stationary distribution for the SIS model, we consider the Forward Kolmogorov Equation,

$$\frac{dp_i(t)}{dt} = \frac{\beta}{N}(i-1)(N-i+1)p_{i-1}(t) + \gamma(i+1)p_{i+1}(t) - \left[\frac{\beta}{N}i(N-i) + \gamma i\right] p_i(t), \tag{3}$$

where $p_i(t) = \mathbb{P}(I(t) = i)$ for $i = 0, 1, ...N$, with $p_{-1}(t) = p_{N+1}(t) = 0 \forall t \geq 0$.

Conditioning upon non-extinction, define $q_i(t) = \mathbb{P}(I(t) = i \mid I(t) > 0)$ for $i = 1, 2, ..., N$, so that $q_i(t) = \frac{p_i(t)}{1-p_0(t)}$. Then

$$\frac{dq_i}{dt} = \frac{(1-p_0(t))\frac{dp_i(t)}{dt} - (p_i(t))\frac{d}{dt}(1-p_0(t))}{(1-p_0(t))^2} = \frac{(1-p_0(t))\frac{dp_i(t)}{dt} + p_i(t)\frac{d}{dt}(p_0(t))}{(1-p_0(t))^2}$$

$$= \frac{(1-p_0(t))(\frac{\beta}{N}(i-1)(N-i+1)p_{i-1}(t) + \gamma(i+1)p_{i+1}(t) - (\frac{\beta}{N}i(N-i)+\gamma i)p_i(t))}{(1-p_0(t))^2} + \left(\frac{p_i(t)}{1-p_0(t)}\right)\left(\frac{\gamma p_1(t)}{1-p_0(t)}\right)$$

$$= \frac{\frac{\beta}{N}(i-1)(N-i+1)p_{i-1}(t) + \gamma(i+1)p_{i+1}(t) - (\frac{\beta}{N}i(N-i)+\gamma i)p_i(t)}{1-p_0(t)} + \left(\frac{p_i(t)}{1-p_0(t)}\right)\left(\frac{\gamma p_1(t)}{1-p_0(t)}\right)$$

$$= \frac{\beta}{N}(i-1)(N-i+1)q_{i-1}(t) + \gamma(i+1)q_{i+1}(t) - \left(\frac{\beta}{N}i(N-i)+\gamma i\right)q_i(t) + q_i(t)\gamma q_1(t) \tag{4}$$

for $i = 1, 2, \ldots, N$ where $q_0(t) = q_{N+1}(t) = 0$. Denoting by Q^C the transition rate matrix Q truncated to remove the first row and column, equation (3) may then be written as

$$\frac{d\boldsymbol{q}}{dt} = \boldsymbol{q}Q^C + \gamma q_1 \boldsymbol{q}. \tag{5}$$

Setting the time derivatives to zero, we find the quasi-stationary probabilities of the SIS system satisfy

$$\frac{\beta}{N}(i-1)(N-i+1)q_{i-1} + \gamma(i+1)q_{i+1} - \left(\frac{\beta}{N}i(N-i)+\gamma i\right)q_i = -\gamma q_1 q_i. \tag{6}$$

That is,

$$\boldsymbol{q}Q^C = -\gamma q_1 \boldsymbol{q}. \tag{7}$$

Where $\boldsymbol{q}$ is the leading left eigenvector of the transition rate matrix, when restricted to non-zero states, Q^C. Figure 1 shows a solution $\boldsymbol{q}$ for $N = 100, \gamma = 1, \beta = 3$. These parameter values demonstrate the normal appearance of the quasi-stationary distribution when it is not concentrated close to $i = 0$ (in particular, $R_0 > 1$).

The hazard rate for extinction is given, at any time t, by $\gamma\mathbb{P}(I(t) = 1|I(t) > 0)$, since extinction can only occur from state $I = 1$, and transitions from $I = 1$ to $I = 0$ occur at rate γ. In quasi-stationarity this hazard rate is γq_1, and remains constant. The time to extinction starting from quasi-stationarity is therefore an exponentially distributed random variable of mean $1/\gamma q_1$.

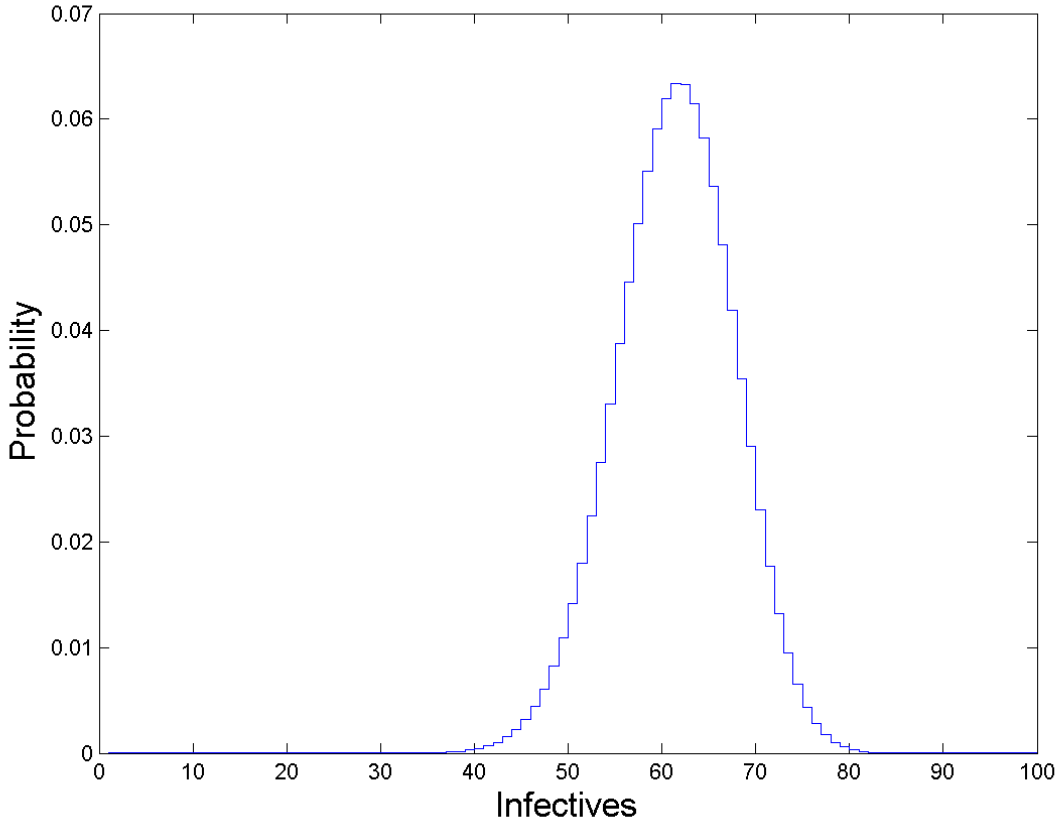

Figure 1: SIS model: example of a quasi-stationary distribution. $N = 100, \gamma = 1, \beta = 3$.

2.2.3 Approximating the time to extinction from quasi-stationarity

Exact derivation of properties of a process can be difficult when exact solutions cannot be calculated. One common diffusion approximation is known as the Ornstein-Uhlenbeck approximation, such as demonstrated by Andersson and Britton (2000). This is a time-homogeneous diffusion process satisfying the stochastic differential equation

$$dx_t = \theta(\mu - x_t)dt + \varsigma dW_t \tag{8}$$

where W_t is a Wiener process, and $\theta > 0, \varsigma > 0$.

The SIS model may first be approximated by the diffusion process $X(t)$ satisfying

$$dX = \left(\frac{\beta}{N}X(N-X) - \gamma X\right)dt + \left(\sqrt{\frac{\beta}{N}X(N-X) + \gamma X}\right)dW \tag{9}$$

where $W(t)$ is standard Brownian motion (see, for example, Ethier and Kurtz (1986), section 11.3).

Close to the deterministic equilibrium point $\left(\text{so } X \simeq N\left(1-\frac{1}{R_0}\right)\right)$ we can further approximate the diffusion (9) by approximating both the drift and diffusion coefficients to leading order in X. This yields the Ornstein-Uhlenbeck process $\tilde{X}(t)$ satisfying

$$d\tilde{X} = -(\beta-\gamma)\left(\tilde{X} - N\left(1-\frac{1}{R_0}\right)\right)dt + \sqrt{2\gamma N\left(1-\frac{1}{R_0}\right)}dW$$

provided $R_0 > 1$. The quasi-stationary distribution of $I(t)$ is then approximated by the stationary distribution of the Ornstein-Uhlenbeck process $\tilde{X}(t)$, resulting in a Gaussian distribution with mean $N\left(1-\frac{1}{R_0}\right)$ and variance Σ which can be calculated by solving the equation

$$2B\Sigma = -S,$$

where B and S are the local drift and variance, $B = -(\beta-\gamma)$ and $S = 2\gamma N\left(1-\frac{1}{R_0}\right)$. We thus find $\Sigma = \frac{N}{R_0}$. Figure 2 shows a plot of this Gaussian distribution, alongside the true quasi-stationary distribution for the same parameter values. They are seen to be in good agreement for these parameter values, as they are for parameter choices resulting in $R_0 > 1$. From this approximation, expected time to extinction can be estimated by considering the amount of time spent close to the extinction state $I = 0$. Taking $\Sigma = N\sigma^2$, that is,

$$\sigma^2 = \frac{1}{R_0}, \tag{10}$$

the probability of being in state $I = 1$ is approximated by

$$\begin{aligned} q_1 = \mathbb{P}(I=1) &= \mathbb{P}(0.5 \le I \le 1.5) \\ &\approx \frac{\varphi\left(\frac{1-Ni^*}{\sigma\sqrt{N}}\right) \times \left(\frac{1.5-0.5}{\sigma\sqrt{N}}\right)}{\phi\left(\frac{Ni^*-0.5}{\sigma\sqrt{N}}\right)} \\ &\approx \frac{1}{\sigma\sqrt{2\pi N}} \exp\left(-\frac{1}{2}\left(\frac{Ni^*-1}{\sigma\sqrt{N}}\right)^2\right). \end{aligned}$$

where $\phi(\cdot)$ and $\varphi(\cdot)$ denote the standard normal distribution function and density function, respectively.

Therefore, the expected time to extinction is approximated as

$$T = \frac{1}{\gamma q_1} \approx \frac{\sigma\sqrt{2\pi N}}{\gamma} \exp\left(\frac{1}{2}\left(\frac{Ni^*-1}{\sigma\sqrt{N}}\right)^2\right). \tag{11}$$

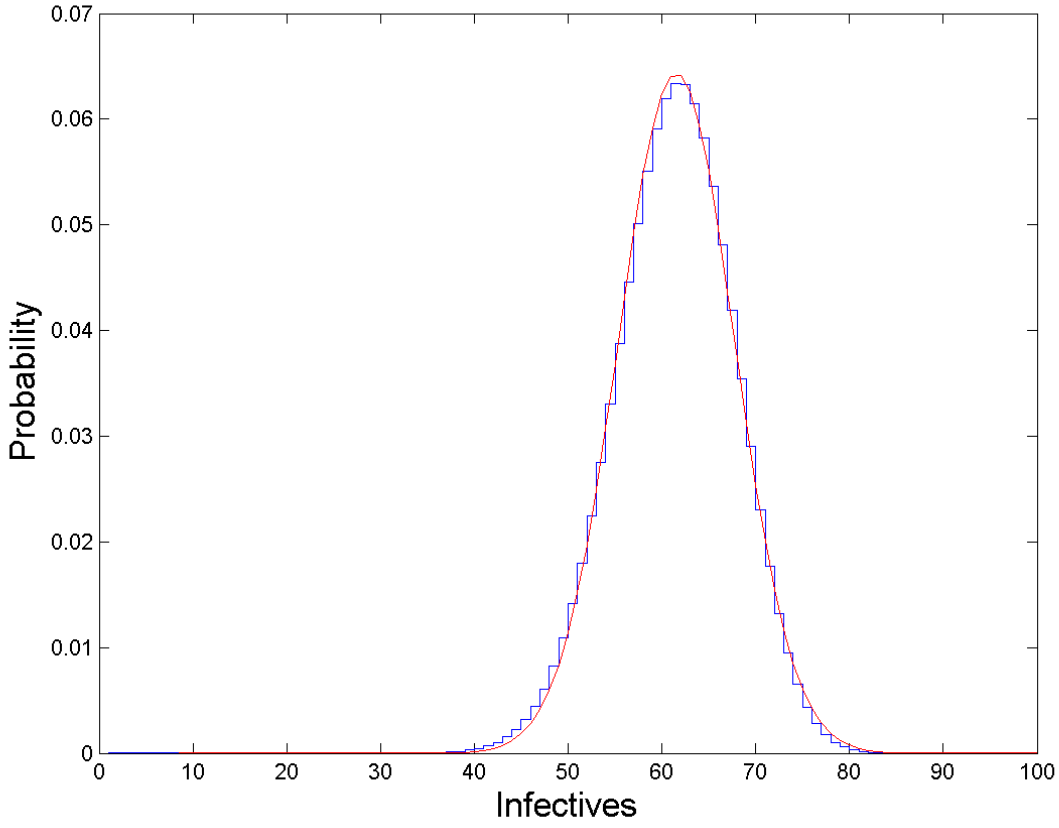

Figure 2: SIS model: example of a quasi-stationary distribution. $N = 100, \gamma = 1, \beta = 3$. Ornstein-Uhlenbeck approximation shown for comparison (red curve).

2.2.4 Approximating the time to extinction from a fixed initial state

By considering a linear system formed by the transition rate matrix of the Markov chain, truncated to the nonzero states, Q^C in (4), the expectation of time to extinction can be calculated for any given initial state. Writing $\boldsymbol{T} = (T(1), T(2), ...T(N))$, where $T(i)$ is the expected time to extinction from state i,then we have

$$Q^C \boldsymbol{T} = -\mathbf{1}, \tag{12}$$

(Norris, 1997, theorem 3.3.3), which can then be solved for $\boldsymbol{T}$.

Recalling the diffusion process $X(t)$ given by (8), and defining

$$T^D(x) = \mathbb{E}\left[\inf\{t \geq 0 : X(t) = 0\} \middle| X(0) = x\right] \text{ for } x \in [0, N],$$

then the expected extinction time $T^D(x)$ satisfies the Kolmogorov backward equation

$$\left(\frac{\beta}{N}x(N-x)-\gamma x\right)\frac{\partial T^D}{\partial x}+\frac{1}{2}\left(\frac{\beta}{N}x(N-x)+\gamma x\right)\frac{\partial^2 T^D}{\partial x^2}=-1 \text{ for } x\in(0,N), \tag{13}$$

with boundary conditions $T^D(0)=0$ and $\left.\frac{\partial T^D}{\partial x}\right|_{x=N}=0$ (Gardiner, 2009, section 5.5.2).

The solution of (4) may be written explictly as

$$T^D(x)=2\int_0^x\frac{dy}{\psi(y)}\int_y^N\frac{\psi(z)}{G(z)}dz \tag{14}$$

where $F(x)=\frac{\beta}{N}x(N-x)-\gamma x$, $G(x)=\frac{\beta}{N}x(N-x)+\gamma x$ and $\psi(x)=\exp\left(\int_0^x dx'[2F(x')/G(x')]\right)$. (Gardiner, 2009, section 5.5.2).

Another approximation of the time to extinction for the SIS model is that made by Andersson and Djehiche (1998). They used asymptotic approximation to calculate a time to extinction as $N\to\infty$. They derived properties of time to extinction τ as $N\to\infty$, as long as the initial number of infectives remained significant, $\frac{I_0}{N}\to\bar{I}>0$. Whilst it is known that from quasi-stationarity time to extinction is exponentially distributed, their derived formula also holds asymptotically for non-quasi-stationary states.

Doering et al (2005) have shown that asymptotically, for large N, the diffusion approximation (14) does not give a good approximation to mean persistence time for the SIS model. Nevertheless, recent papers (Doubova and Vadilo, 2016; Wang et al, 2014) have used such a diffusion to approximate persistence time. Since we are interested in small/moderate population sizes, and since others are making use of the diffusion approximation, we will include it as one of the methods we study.

The formula for expected time to extinction of Andersson and Djehiche (1998) is:

$$E(\tau)\sim\frac{1}{\gamma}\sqrt{\frac{2\pi}{N}}\frac{\beta}{(\beta-1)^2}e^{N(log\beta-1+\frac{1}{\beta})}. \tag{15}$$

They also give time to extinction formulae for cases of $R_0\leq 1$ (in their model denoted λ), as $N\to\infty$, however as stated before this is of less interest due to the much shorter time that the process persists. In the case where the number of infectives does not vanish, $I_o/N\to\bar{a}>0$ as $N\to\infty$, and with $\gamma=1$, the

time to extinction, τ, satisfies

$$(1-\beta(1-\bar{a}))\tau - \log N - \log \bar{a} - \log(1-\beta(1-\bar{a})) \to W, \text{ where } \mathbb{P}(W \leq w) = \exp\{-e^{-w}\}. \tag{16}$$

The time to extinction can also be approximated by a linear birth-death process approximation, approximating the infective process $I(t)$ in the SIS model by a birth-death process with birth rate βI and death rate γI. This is equivalent to assuming $S(t) \approx N \forall t$, such that birth and death rates become linear functions of I.

The formula for mean time to extinction of a birth-death process is given as equation (7.10) in chapter 4 of Karlin and Taylor (1975) "A First Course in Stochastic Processes, 2nd edition". For a birth and death process with birth parameters λ_n and death parameters μ_n, $n \geq 1$, where $\lambda_0 = 0$, the absorbing state, the mean time to absorption from initial state m is

$$\begin{cases} \infty & \text{if } \sum_{i=1}^{\infty} \rho_i = \infty, \\ \sum_{i=1}^{\infty} \rho_i + \sum_{r=1}^{m-1} \left(\prod_{k=1}^{r} \frac{\mu_k}{\lambda_k} \right) \sum_{j=r+1}^{\infty} \rho_j & \text{if } \sum_{i=1}^{\infty} \rho_i < \infty, \end{cases} \tag{17}$$

where $\rho_i = (\lambda_1 \lambda_2 \cdot \ldots \cdot \lambda_{i-1})/(\mu_1 \mu_2 \cdot \ldots \cdot \mu_i)$.

Taking $\lambda_n = \beta n$ and $\mu_n = \gamma n$, we find time to extinction for the linear birth-death process approximating the SIS model from an initial state m is

$$\tau = \log(1-R_0)\left(1-\frac{1}{R_0}\right)^m + \sum_{i=1}^{m} \frac{1}{i} - \frac{1}{R_0^m(\gamma-\beta)} \sum_{i=1}^{m} \frac{R_0^i}{i}. \tag{18}$$

2.3 SIR epidemic model with demography

Demography provides an additional complication to the model, but in the simplest fashion. It is unrealistic to consider an unaging immortal population, especially with many diseases where the effect on mortality is one of the main features in its time to extinction, or in general the reason it is of interest. One of the simplest models to incorporate this feature is the SIR model with demography, sometimes called the Martini model. In this model, immigration/birth and emigration/death processes are incorporated. The deterministic version of this model has been studied by Martini (1921), and many others. The stochastic version of this model has been studied by van Herwaarden and Grasman (1995), Andersson and Britton (2000) and Nåsell (1996, 2002 and 2005) as well as many others.

In this model, individuals are born/immigrate into the population at a constant rate μN. Each individual has an exponentially distributed lifetime with intensity μ, i.e. the average lifetime is given by $1/\mu$. This results in a population size that fluctuates about the value N. Transition rates are as follows.

Event	State transition	Transition rate
Birth/Immigration	$(S, I) \to (S+1, I)$	μN
Death/Removal of susceptible	$(S, I) \to (S-1, I)$	μS
Death/Removal of infected	$(S, I) \to (S, I-1)$	$(\mu+\gamma)I$
Infection	$(S, I) \to (S-1, I+1)$	$\frac{\beta}{N}SI$

Here $\mu > 0$ represents the rate of demography, for birth and death, and $\gamma > 0$ is the additional rate of death (or recovery) for infected individuals. The basic reproduction number is $R_0 = \dfrac{\beta}{\gamma+\mu}$. It is also useful to consider deadliness $\alpha = \dfrac{\mu+\gamma}{\mu}$, the measure of relative rate leaving active population (S, I).

Here, all states $(s, 0)$ communicate with each other, but not with any other state (s, i) where $i \geq 1$. These states $\{(s, 0) : s = 0, 1, 2, ...\}$ therefore form an absorbing class, with all other states transient. The Kolmogorov Forward equation for this model, with $p_{s,i}(t) = \mathbb{P}((S(t), I(t)) = (s, i))$, is then

$$\begin{aligned}\frac{dp_{s,i}}{dt} =&\mu N p_{s-1,i}(t) + \frac{\beta}{N}(s+1)(i-1)p_{s+1,i-1}(t) + \mu(s+1)p_{s+1,i}(t) \\ &+ \mu(i+1)p_{s,i+1}(t) + \gamma(i+1)p_{s,i+1}(t) - \left(\mu N + \frac{\beta}{N}si + \mu s + \mu i + \gamma i\right) p_{s,i}(t)\end{aligned} \tag{19}$$

where $s = 0, 1, 2, ...$ and $i = 0, 1, 2, ...$

2.3.1 Deterministic model

We scale the process $\frac{1}{N}(S(t), I(t)) = (s(t), i(t))$, as before. The deterministic model of the scaled process is given by

$$\frac{ds}{dt} =\mu(1-s) - \beta si, \tag{20}$$

$$\frac{di}{dt} =\beta si - (\mu+\gamma)i. \tag{21}$$

There are two stationary points, that of the extinction $(1, 0)$, resulting in a disease free state, and that of an endemic state,

$$(s^*, i^*) = \left(\frac{1}{R_0}, \frac{R_0 - 1}{\alpha R_0}\right), \tag{22}$$

similar to the endemic states seen in other models. It can be shown that the first stationary point is stable when $R_0 < 1$ and unstable when $R_0 > 1$, while the second stationary point is unfeasible when $R_0 < 1$, and stable when $R_0 > 1$ (Nåsell, 2002).

2.3.2 Stochastic model

As with the SIS model, the SIR model with demography can also be considered to have a limiting conditional distribution, and to calculate our quantities of interest involving the quasi-stationary distribution, we must first condition on non-extinction. The state probabilities denoted $q_{s,i}(t)$ are conditioned on non-extinction, and can be determined via their relation to the unconditioned probabilities $p_{s,i}(t)$.

$$\begin{aligned} q_{s,i}(t) &= \mathbb{P}\big(S(t)=s, I(t)=i \mid I(t)>0\big) \text{ for } s=0,1,\dots \text{ and } i=1,2,\dots \\ &= \frac{p_{s,i}(t)}{1-p_{\bullet 0}(t)}, \end{aligned} \tag{23}$$

where $p_{\bullet i}(t)$ is the marginal distribution of the number of infected individuals i at time t, and is given by

$$p_{\bullet i}(t) = \sum_{s=0}^{\infty} p_{s,i}(t) = P\{I(t)=i\}. \tag{24}$$

Summing the Kolmogorov forward equations (20)for the states $i=0$ and all non-negative values of s, we obtain the differential equation

$$p'_{\bullet 0}(t) = (\mu+\gamma)p_{\bullet 1}(t). \tag{25}$$

Differentiating equation (23) and using (25) gives

$$q'_{s,i}(t) = \frac{p'_{s,i}(t)}{1-p_{\bullet 0}(t)} + (\mu+\gamma)\frac{p_i(t)}{(1-p_{\bullet 0})^2}. \tag{26}$$

Differential equations for $q_{s,i}$, the conditional state probabilities can then be derived

$$\begin{aligned} \frac{dq_{s,i}}{dt} =& \mu N q_{s-1,i}(t) + \frac{\beta}{N}(s+1)(i-1)q_{s+1,i-1}(t) + \mu(s+1)q_{s+1,i}(t) + \mu(i+1)q_{s,i+1}(t) \\ &+ \gamma(i+1)q_{s,i+1}(t) - \left(\mu N + \frac{\beta}{N}si + \mu s + \mu i + \gamma i\right) q_{s,i}(t) + (\mu+\gamma)q_{\bullet 1}q_{s,i}(t) \end{aligned} \tag{27}$$

where $s=0,1,2,\dots$ and $i=1,2,\dots.$ The quasi-stationary distributon $q_{s,i}$ is the statonary solution of this system of differential equations.

Models with demography allow for unbounded immigration, and therefore infinite state space. This can cause issues when attempting to calculate theoretical quantities such as the expected time to extinction exactly, as matrices of infinite size are not generally tractable. Truncation of this state space at an appropriate point allows for the calculation of results, with minimal impact on the resulting expectation, provided the truncation is chosen appropriately.

2.3.3 Approximating the time to extinction from quasi-stationarity

As with the SIS model, a common approximation of the SIR model with demography is that of an Ornstein-Uhlenbeck process. First, we scale and centre the process, creating the process $(\bar{S}^N(t), \bar{I}^N(t)) = (S(t) - Ns^*, I(t) - Ni^*)/\sqrt{N}$. We then approximate the process by a two-dimensional Ornstein-Uhlenbeck process, as in Ethier and Kurtz (1986). This produces the limiting process $(\bar{S}(t), \bar{I}(t))$, whose stationary distribution is bivariate Gaussian, with mean $(0, 0)$ and covariance matrix Σ, where Σ is the matrix solving

$$\boldsymbol{J}(s^*, i^*)\Sigma + \Sigma \boldsymbol{J}(s^*, i^*)^T = -\boldsymbol{G}(s^*, i^*) \tag{28}$$

as shown in Gardiner (1985), where $\boldsymbol{J}(s^*, i^*)$ and $\boldsymbol{G}(s^*, i^*)$ are the local drift and covariance matrices of $(\bar{S}(t), \bar{I}(t))$ respectively. The local drift matrix is the Jacobian matrix of the first order infinitesimal moments of the scaled process, and the local covariance matrix is the infinitesimal covariance matrix of the scaled process. For this approximation we evaluate $\boldsymbol{J}(s, i)$ and $\boldsymbol{G}(s, i)$ at the endemic level, as that is the area in which its behaviour is most interesting. This results in

$$\boldsymbol{J}(s^*, i^*) = \begin{pmatrix} -\beta i^* - \mu & -\beta s^* \\ \beta i^* & \beta s^* - (\gamma + \mu) \end{pmatrix} = \begin{pmatrix} -\mu R_0 & -\mu\alpha \\ \mu(R_0 - 1) & 0 \end{pmatrix} \tag{29}$$

and

$$\boldsymbol{G}(s^*, i^*) = \begin{pmatrix} \beta s^* i^* + \mu(1 + s^*) & -\beta s^* i^* \\ -\beta s^* i^* & \beta s^* i^* + (\gamma + \mu) i^* \end{pmatrix} = \frac{\mu}{R_0} \begin{pmatrix} 2R_0 & -(R_0 - 1) \\ -(R_0 - 1) & 2(R_0 - 1) \end{pmatrix} \tag{30}$$

for $R_0 > 1$.

The stationary distribution of the process $(\bar{S}(t), \bar{I}(t))$ can then be used to provide an approximation of the quasi-stationary distribution of (S, I), and therefore be used to estimate time to extinction of the original process. The stationary distribution is bivariate normal, with mean $N(s^*, i^*)$, and covariance matrix $N\Sigma$. An explicit expression for the covariance matrix can be derived, giving the solution

$$\Sigma = \frac{1}{R_0^2} \begin{pmatrix} \alpha + R_0 & -R_0 \\ -R_0 & R_0 - 1 + R_0^2/\alpha \end{pmatrix}. \tag{31}$$

As before, we assume that the scaled discrete process is sufficiently approximated by a continuous process (Nåsell 1999).

The normal distribution approximation relies on a truncation at 0.5, accounting for $I(t) \geq 1$, the number of infected individuals in quasi-stationarity. With this modification, it can be shown that

$$q_{\cdot 1} \approx \frac{\varphi\left(\frac{1 - Ni^*}{\sigma\sqrt{N}}\right) \times \left(\frac{1.5 - 0.5}{\sigma\sqrt{N}}\right)}{\phi\left(\frac{Ni^* - 0.5}{\sigma\sqrt{N}}\right)}, \tag{32}$$

where Ni^* and $\sigma\sqrt{N}$ are the mean and standard deviation of the marginal distribution of the number of infected individuals in the quasi-stationary state, and φ and ϕ respectively denote the normal density and normal distribution function (Nåsell, 2002).

2.4 Additional models

2.4.1 Non-exponential infectious periods and latency

The vast majority of endemic disease models make the implicit assumption that each individual's infectious period follows an exponential distribution. This is purely a mathematical convenience, not motivated by biological realism. We can improve the biological realism of the model by allowing infectious periods to follow an Erlang distribution, using the 'method of stages' (Cox and Miller, 1965). That is, when an individual becomes infected, they pass through k infectious stages, remaining in each stage for an exponentially distributed time of mean $(k\gamma)^{-1}$, before returning to susceptibility. Thus the total infectious period follows an Erlang distribution with mean γ^{-1} and variance $(k\gamma^2)^{-1}$. For instance, the SIS model with Erlang distributed infectious periods can be modelled as a Markov chain $(I_1(t), ..., I_k(t))$with state space $\{i_1, i_2, ..., i_k \geq 0 : \sum_{m=1}^{k} i_m \leq N\}$.

The basic SEIR model as studied by van Herwaarden and Grasman (1995) adds a latent (or 'exposed')

period to the SIR model. Individuals transition $S \to E \to I \to R$, allowing an individual to be affected by the disease, but not instantaneously infective. The transition rates are as follows.

Event	State transition	Transition rate
Birth/Immigration	$(S, E, I) \to (S+1, E, I)$	μN
Death/Removal of susceptible	$(S, E, I) \to (S-1, E, I)$	μS
Infection	$(S, E, I) \to (S-1, E+1, I)$	$\frac{\beta}{N} SI$
Death/Removal of exposed	$(S, E, I) \to (S, E-1, I)$	μE
Progression of disease	$(S, E, I) \to (S, E-1, I+1)$	λE
Death/Removal of infected	$(S, E, I) \to (S, E, I-1)$	$(\mu + \gamma) I$

Here $\mu, \gamma, \lambda, \beta > 0$, are the rates of demography, additional infective death, rate of leaving the latent phase and infection respectively. For this model, the basic reproduction number is $R_0 = \dfrac{\beta\lambda}{(\gamma+\mu)(\lambda+\mu)}$.

The model studied by Andersson and Britton (2000) is a variation on this model: their model also split each of the S, E and I stages up into several substages, making the amount of time that an individual spends in each of these overall stages Erlang distributed, in the same fashion as Anderson and Watson (1980).

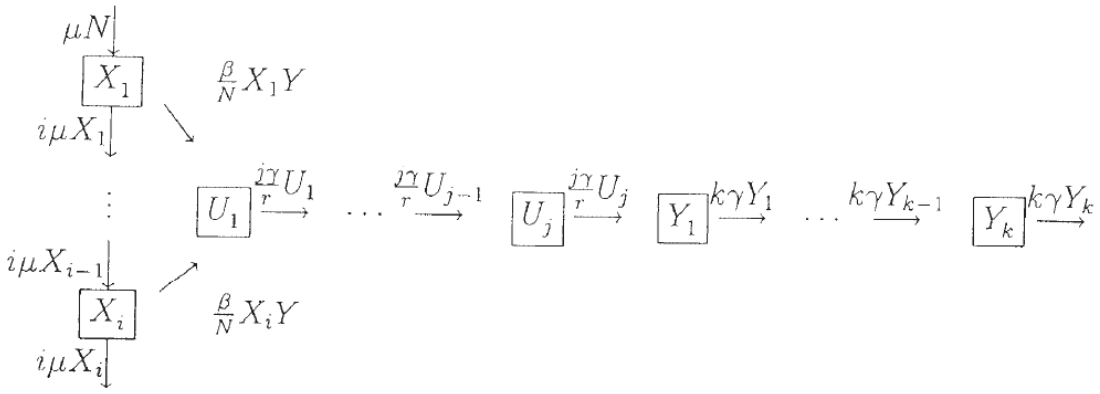

Figure 3: Transition rates of model studied by Andersson and Britton (2000), reproduced from Fig.1 of Andersson and Britton (2000)

Each of the stages S, E, I has i, j, k substages respectively, the numbers of individuals in each substage being labelled $(X_1, X_2, ..., X_i), (U_1, U_2, ..., U_j), (Y_1, Y_2, ..., Y_k)$. An individual may transition from any susceptible stage to exposed, and thereafter transitions through all exposed and infected stages before being removed. An individual may alternatively become removed at the end of all susceptible stages. To make the mathematics tractable, simplifications were made, restricting the effects of death or removal of latent and infected individuals; such effects were considered negligible, as shown in figure 3.

Andersson and Britton (2000) consider primarily the case where the ratio of latent and infectious periods to life-length is small. Denoting by r the relative expected length of the latent period with respect to the infectious period, and defining $\epsilon = \gamma^{-1}/\mu^{-1}$, the ratio of infectious period to life-length, the case of $(1 + r)\epsilon < 1$ is studied. In simulation, low values such as $\epsilon = \frac{1}{3640}$ were used. This acts as justification for the negligible chance of death whilst latent or infective. Van Herwaarden and Grasman (1995) do not use these parameter values in their similar model, so their results are markedly different.

The model is first approximated by considering ρ, the chance that given there is only a single infective remaining, they are in the final infectious stage. This is done by considering the time spent in each visit to this state, assuming the susceptible level always remains at the level of endemic equilibrium.

The model is then approximated using an $(i + j + k)$ dimensional Ornstein-Uhlenbeck diffusion process, due to the model being otherwise intractable. The local drift and covariance matrices B and S are reduced from their full form by assuming ϵ small, and neglecting insignificant terms, before calculating

Σ, the variance matrix of the stationary distribution, as in simpler models, using equation (29).

The impact of the parameters R_0, ϵ, r are assessed with respect to persistence, as well as the coefficients of variation of each of the S, E, I stages. Increases in ϵ, r, Coefficient of Variation of latent and infectious periods were found to cause a monotonic increase in τ, the time to extinction, whilst trends for R_0 (here denoted R) and the Coefficient of Variation of life length were only consistent within specific ranges of N.

Parameter	Type value	Parameter range	Monotone $N=10^5$	Monotone $N=10^6$	τ range $N=10^5$	τ range $N=10^6$	Rel. change $N=10^5$	Rel. change $N=10^6$
R	15	5–20	↘	↗	3.2–5.4	22–41	0.6	1.8
ϵ	0.0003	0.00015–0.0006	↗	↗	1.6–10.3	15–525	6.4	35
r	0.5	0–2	↗	↗	2.4–11.6	11–2000	4.9	170
CV_{life}	0.3	0–1	↘	↗	3.4–3.6	31–36	0.96	1.1
CV_{lat}	0.5	0–1	↗	↗	3.5–3.6	31–36	1.01	1.1
CV_{inf}	0.5	0–1	↗	↗	3.5–3.7	26–45	1.08	1.5
v	0	0–0.9	↘	↘	1.7–3.6	5–32	0.46	0.17

Table 1: Results of approximation, reproduced from Andersson and Britton (2000) Table 1.

With some exceptions, the dependence on parameters was largely monotonic. However, some of these trends appear to be non monotonically increasing or decreasing in N, that is to say there are different results for $N = 10^5$ and $N = 10^6$. Cases of non-monotonicity with respect to variables is gnerally reserved for cases where R_0 is high, causing the epidemic to quickly infect everyone and "burn out", causing a short extinction time as opposed to its normal effect. For the population sizes being considered in this instance, this is unlikely, and may be an error based on a poor Ornstein-Uhlenbeck approximation. If the process is insufficiently normal, then errors can occur in this multi-stage approximation. The trends of R and CV_{life} are listed here as non-monotonic.

2.4.2 Multi-group models

Hagenaars et al.(2004) considered a modified SIR model with demography, which was used to study the impact of spatial heterogeneity on persistence. This model consists of n patches, each comprising N individuals, and has the following transition rates, for each patch.

Event (for patch i)	State transition	Transition rate
Birth/immigration of susceptible	$(S_i, I_i, R_i) \to (S_i + 1, I_i, R_i)$	$\mu N - \mu\lambda_E$
Death/emigration of susceptible	$(S_i, I_i, R_i) \to (S_i - 1, I_i, R_i)$	μS_i
Infection of susceptible	$(S_i, I_i, R_i) \to (S_i - 1, I_i + 1, R_i)$	$\beta S_i \frac{I_i + \varepsilon \Sigma_{i \neq j} I_j}{N(1 + \varepsilon(n-1))}$
Immigration of infected	$(S_i, I_i, R_i) \to (S_i, I_i + 1, R_i)$	$\mu\lambda_E$
Death/emigration of infected	$(S_i, I_i, R_i) \to (S_i, I_i - 1, R_i)$	μI_i
Recovery of an infected	$(S_i, I_i, R_i) \to (S_i, I_i - 1, R_i + 1)$	vI_i
Death/emigration of recovered	$(S_i, I_i, R_i) \to (S_i, I_i, R_i - 1)$	μR_i

Here $\beta, \mu, \lambda_E, v > 0$, representing rates of infectivity, demography, immigration of infectives and recovery respectively.

This model does not allow for the movement of individuals between patches, but does allow for the infection of individuals between patches. For this model, $R_0 = \frac{\beta}{\mu\alpha}$, where $\alpha = (1 + \frac{v}{\mu})$. Notably, R_0 does not depend on the spatial heterogeneity parameter ε, so the effects of patch size and number of patches on persistence time can be studied separately.

The effects of R_0, N, α and ε (relative contact rate between patches) on persistence time were considered and measured, along with the dynamics behind such effects, such as 'Rescue effects' which reintroduce infection to a subpopulation where the infection would otherwise go extinct. A patch where the disease is already extinct may have individuals infected by other patches, allowing for another local outbreak.

Hagenaars et. al (2004) go on to approximate the process of extinction, and analyse the patch-based model assuming that each of these patches jump from an endemic state to one of full susceptibility instantaneously, an assumption justified in cases of small α (ratio of infectious period to life length), where immunity is quickly lost. This results in the following transition rates.

Number of infected patches	Transition rate
$j \to j+1$	$(n-j)j\varepsilon N \dfrac{\mu R_0}{1+\varepsilon(n-1)} \left(1-\dfrac{1}{R_0}\right)^2$
$j \to j-1$	$\dfrac{j}{\tau_N}$

Here τ_N represents the expected time to extinction of infection for a single patch of size N without influence from any other patches.

Only values of $n = 2, 10$ were considered for simplicity. It was found that if transmission potential was kept fixed, an increase in the level of spatial heterogeneity typically results in a decrease in disease persistence.

Lindholm and Britton (2007) attempt to reconcile the problems with large α (incredibly short periods of immunity) by introducing a period of temporary immunity after recovery, resulting in an SIRS model for patches, with the following transition rates.

Patch transition	Transition rate
$S \to I$	$SI\varepsilon N \dfrac{\mu N R_0}{1+\varepsilon(n-1)} \left(1-\dfrac{1}{R_0}\right)^2$
$I \to R$	$\dfrac{S}{\tau_N}$
$R \to S$	$\dfrac{n-(S+I)}{\tau_R}$

Here, S is the number of of susceptible patches, I is the number of patches in the infected state and τ_R is the length of time that a patch remains immune; $\epsilon, n, R_0 > 0$ are the proportion of contacts an individual has which are with members of a different community, the number of subgroups in the community, and the basic reproduction number, respectively.

A formula for mean time to extinction in terms of n was found, however this result could not be evaluated analytically. From numerical evaluation, it was concluded that increases in spatial heterogeneity led to a decrease in disease persistence for this model, but that increasing the degree of social interaction ϵ resulted in an increased persistence time. The parameter values used for these results were α value $\alpha = 3500, R_0 = 14, n \in [3, 5]$, a notably high α value.

2.4.3 Models with logistic birth

'Logistic birth' refers to a model with a carrying capacity that the population will automatically settle towards, with greater birth if significantly below, reducing as carrying capacity is reached; this results from a birth rate in the form of a logistic curve. Population is again variable, with N, the total number of individuals, not constant. The transition $N \to N+1$ occurs at rate $\left(b - r\frac{N}{K}\right)N$, where K is the carrying capacity, and constants $b, r > 0$, while the transition $N \to N-1$ occurs at rate dN, $0 < d < b$.

The SIS model with logistic birth has been studied both deterministically and stochastically (Nåsell (2001)), whilst the SIR and SIRS models with logistic birth have only been studied deterministically (Gao and Hethcote (1992), Yoshida and Hara (2006)). Kryscio and Lèfevre(1989) note that the expectation of time to extinction for the stochastic model does not exactly match that of the deterministic model, and may produce distinctly larger results in the case of $R_0 >> 1$.

The SIR model with logistic birth has transition rates as follows.

Event	State transition	Transition rate
Birth/immigration of susceptible	$(S, I, R) \to (S+1, I, R)$	$\left(b - r\frac{N}{K}\right)N$
Death/emigration of susceptible	$(S, I, R) \to (S-1, I, R)$	dS
Infection of susceptible	$(S, I, R) \to (S-1, I+1, R)$	$\frac{\beta SI}{N}$
Death/emigration of infected	$(S, I, R) \to (S, I-1, R)$	dI
Recovery of an infected	$(S, I, R) \to (S, I-1, R+1)$	λI
Death/emigration of recovered	$(S, I, R) \to (S, I, R-1)$	dR

Here $N(t) \equiv S(t) + I(t) + R(t)$ and $b, r, K, d, \beta, \lambda > 0$ are constant parameters. Here, b and r represent the birth/immigration rate of the population, relative to K, the carrying capacity of the population, d represents the death/emigration rate of the population, which remains constant throughout the stages of infection, β represents the rate of infection and λ represents the rate of recovery. The dependence of the birth rate on the carrying capacity is represented by r, also known as the density dependence.

As the fraction of density dependence varies, disease related deaths either lower the asymptotic population size, or cause the population to approach extinction. For where the net growth threshold $\phi \leq 1$ is exceeded by the death rate, extinction can occur rapidly in even cases of high R_0. There are no disease

related deaths in this model

Here, ϕ is defined as $\phi = \dfrac{r\lambda}{\alpha[\lambda - (y + \alpha + d)]}\left(1 + \dfrac{\gamma}{\delta + d}\right)$.

The region of interest in this model may not be limited to high α unlike other models, due to its similarity to predator-prey models, for different parameter values.

3 SIS/SIR model approximation comparisons

3.1 Brief discussion of models

The SIS and SIR models are amongst the simplest of models of endemic disease to consider. Despite this simplicity, they share many of the more complicated properties of dieases. The SIS model is generally speaking more amenable to analysis due to the restricted finite state space, and as a result many of the approximations of the SIS model are unnecessary, but do provide valuable insight into the flaws of such approximations for situations where the exact solution cannot so easily be calculated.

3.1.1 Approximations of the SIS Model

We first consider the deterministic version of the SIS model of section 2.2, producing a simple approximation to time to extinction. For any initial state $i(0) > 0$, the solution to (1) satisfies $i(t) > 0$ for all $t \geq 0$, so that extinction never occurs. However, equation (1) is a continuous approximation to a discrete-state process. Hence the natural continuity correction is to identify the state $I(t) = 0$ with the interval $i(t) \leq \frac{1}{2N}$, and to define the extinction time

$$T^{Det}(x) = \inf\left\{t \geq 0 : i(t) \leq \frac{1}{2N}\right\} \text{ for } i(0) = x.$$

Solving equation (1), we find

$$i(t) = \frac{x\,(\beta - \gamma)}{x\beta - x\beta e^{-(\beta-\gamma)t} + \beta e^{-(\beta-\gamma)t} - \gamma e^{-(\beta-\gamma)t}}, \tag{33}$$

where xN is the initial number of infectives, which is not required to be an integer. Now for $R_0 > 1$, we have $i(t) \to i^* > 0$ as $t \to \infty$, so that for all sufficiently large N, $T^{Det}(x) = \infty$. On the other hand, for $R_0 \leq 1$ we have $i(t) \to 0$ as $t \to \infty$ and hence $T^{Det}(x) < \infty$ for large N. Now setting $i(t) = \frac{1}{2N}$ in (33) we find, for $R_0 > 1$,

$$T^{Det}(x) = \frac{1}{\gamma - \beta} \ln\left(\frac{x\,(2\beta N - 2\gamma N - \beta)}{-\beta x + \beta - \gamma}\right). \tag{34}$$

3.1.2 Diffusion Approximation

We consider the diffusion approximation of general form

$$A(x)\frac{\partial T(x)}{\partial x} + \frac{1}{2}B(x)\frac{\partial^2 T(x)}{\partial x^2} = -1 \tag{35}$$

with one absorbing boundary (at the state $i = 0$), and one reflecting boundary (at the state $i = N$). That is, $T(0) = 0$, and $\frac{\partial}{\partial x}T(N) = 0$. Here $A(x)$ is the drift matrix, and $B(x)$ is the variance matrix. For the SIS model, these are respectively

$$A(x) = \frac{\beta}{N}(N - x)x - \gamma x$$
$$\text{and } B(x) = \frac{\beta}{2N}(N - x)x + \frac{\gamma}{2}x,$$

as seen in section 2.2.4, and in Gardiner, who finds the solution to be

$$T(x) = 2\int_a^x \frac{dy}{\psi(y)}\int_a^y \frac{\psi(z)}{B(z)}dz \text{ where}$$
$$\psi(x) = \exp\Big\{\int_0^x dx'[2A(x')/B(x')]\Big\}.$$

3.1.3 Approximations of the SIR Model

One of the primary complications in dealing with models with demography such as the SIR model with demography is that they allow for potentially unlimited immigration/birth. Although the models are typically tied to a central tendency, justified by a carrying capacity, the possibilities of large numbers of susceptibles/infectives are nonzero, even though they may be low. Truncations of this state space are therefore a useful tool to approximate the system, especially since the exact calculation of the quasi-stationary distribution for the system is not possible - the matrices required are infinite. We use truncations S_{max} and I_{max} to set the maximum number of S and I respectively that can exist at any given point in time. These values must be taken quite large, and well above the expected equilibrium level of susceptibles and infectives to avoid inaccurate results, as deviations from the mean can be very large, and still contribute to the overall shape of the distribution.

In Figure 4, the distribution of simulated times to extinction is compared with exponential distributions (predicted by theory) whose means are computed by solving the eigenvalue equation (7) using truncated versions of the (infinite) matrix Q^C. The non-truncated simulation is started from the integer values closest to the deterministic equilibrium. The truncation at $S_{max} = I_{max} = 30$ is a poor fit, and does not match the simulated distribution of time to extinction; the shorter truncation inaccurately predicts much shorter times to extinction. The truncations at $S_{max} = I_{max} = 100, 150$ are much better fits,

with there being very little difference between them. This demonstrates the diminishing effect that the truncation has, as it becomes increasingly unlikely for the process to reach such states. Larger values of S_{max} and I_{max} are more accurate, but take increasingly long times to compute. Even for large values of S_{max} and I_{max}, the plot does not perfectly align on the left hand side, as simulation started from integer values closest to the deterministic equilibrium is not perfectly aligned with theoretical results starting from the quasi-stationary distribution.

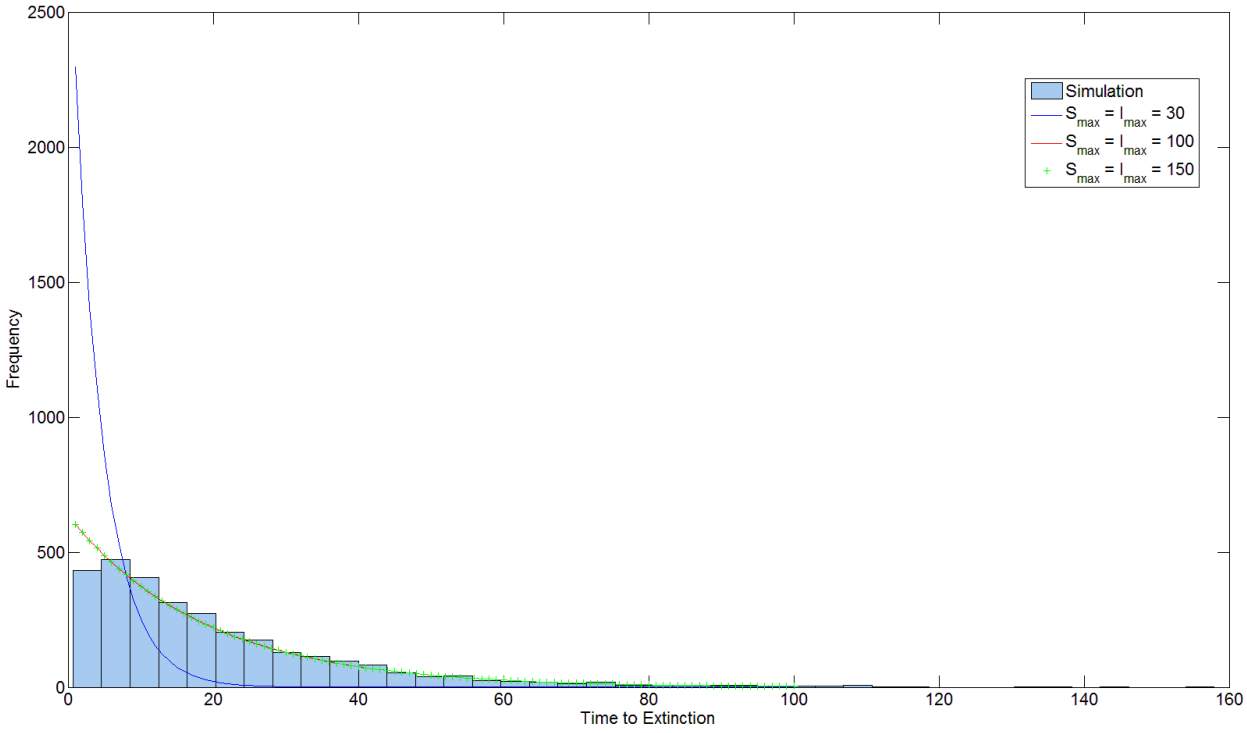

Figure 4: SIR model with demography: simulated time to extinction, compared with exponential distribution of time to extinction from quasi-stationarity with expectation calculated using truncations $S_{max} = I_{max} = 30, 100, 150$, with parameter values $N = 50, \mu = 0.9, \gamma = 1.1, \beta = 2, R_0 = 1$

3.2 Graphs and comparisons

3.2.1 Time to extinction from fixed initial states

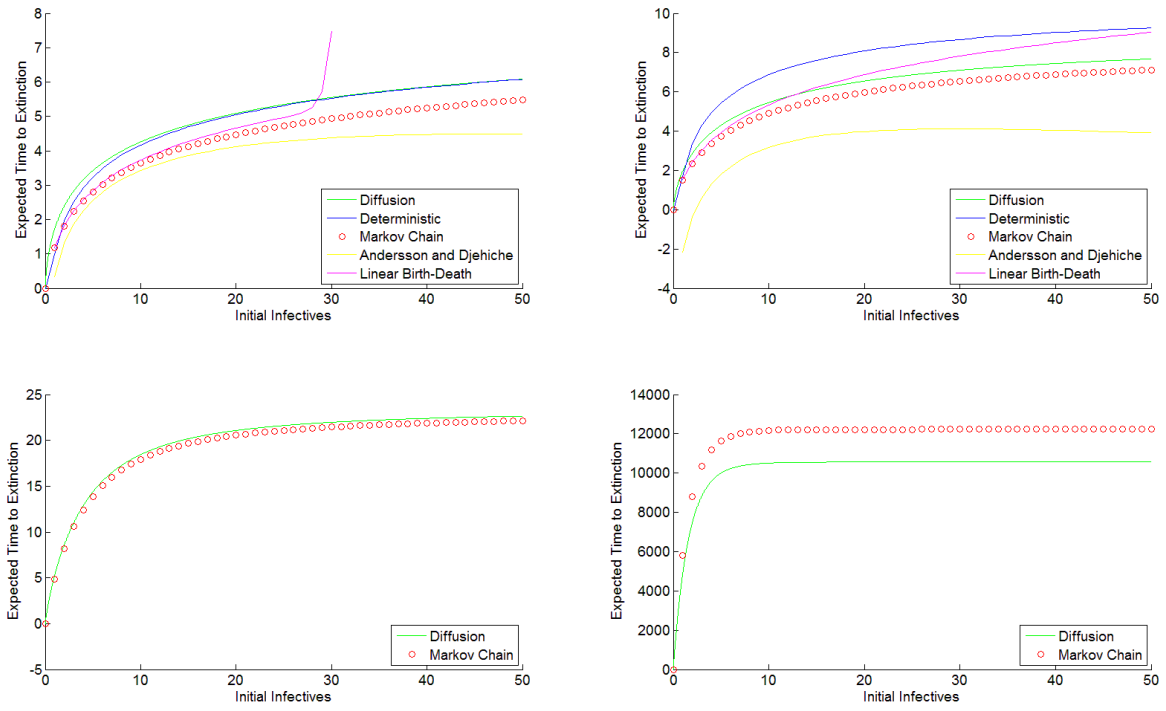

Figure 5: Expected time to extinction from different initial states for the SIS model, with approximations. $N = 50$, $\gamma = 1$. $\beta = 0.3, 0.6, 1.2$ and 2 respectively.

In Figure (5), the time to extinction is considered based on a variety of initial states. The variety of initial states is the number of initially infected individuals in a system, and the process is left to evolve based on fixed parameters for N and γ, whilst a variety of graphs are drawn for different values of β. As I have taken $\gamma = 1$ in all of these graphs, R_0 values are equivalent to β values; in general, this is permissable as scaling a model by γ merely changes the timeframe of study. This allows the approximations to be judged in the most varied conditions, as R_0 is very important parameter with respect the behaviour of the SIS model process.

Figure (5) makes use of equations (12), (14),(16), (18) and (34), and shows how well each approximation does for a variety of values of β. Several of the approximations do not even predict extinction in the case of $R_0 > 1$, such as the deterministic approximation. Note that as $I(0)$ increases, the time to extinction reaches a plateau; each extra initial infective affects the system less.

For low values of β, the diffusion and deterministic approximations consistently overestimate the expected time to extinction. However, for larger values of β the diffusion approximation underestimates the time to extinction whilst the deterministic approximation contrastingly expects no extinction at all, an effectively infinite amount of time. All approximations produce similar values for low initial infectives, but deviate increasingly as the entire population becomes infected. This is expected as several approximations are derived based on behaviour about the endemic equilibrium, typically less than half the value of N. The diffusion and markov chain approximations are close to parity near $R_0 = 1$. For $R_0 > 1$, diffusion underestimates time to extinction. For a low value of β, the linear birth-death processs deviates wildly, due to it relying on the assumption of $S(t) \approx N$.

3.2.2 Time to extinction from quasi-stationarity

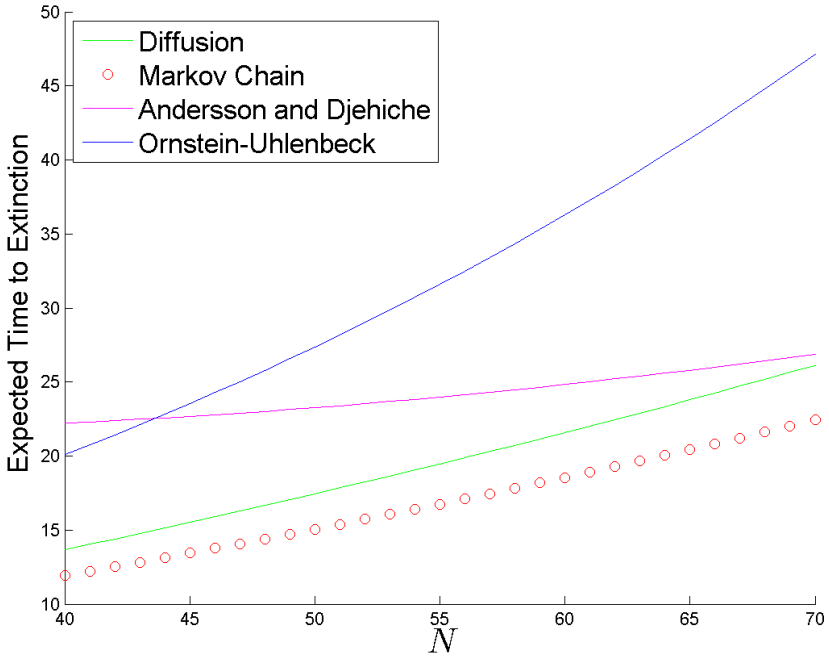

Figure 6: Expected time to extinction from quasi-stationarity for the SIS model, with approximations. $\beta = 1.2$, $\gamma = 1$, $N \in [40, 70]$.

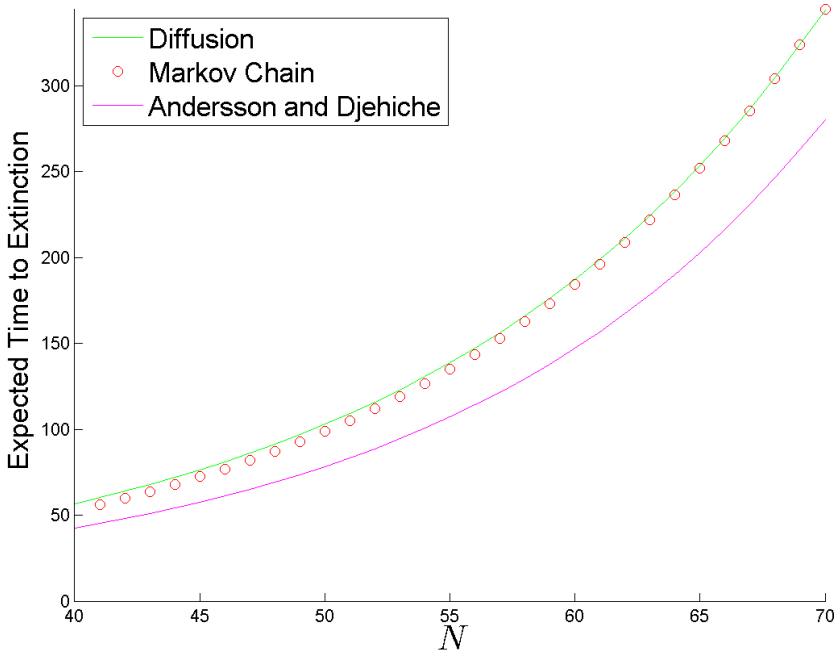

Figure 7: Expected time to extinction from quasi-stationarity for the SIS model, with approximations. $\beta = 1.5$, $\gamma = 1$, $N \in [40, 70]$.

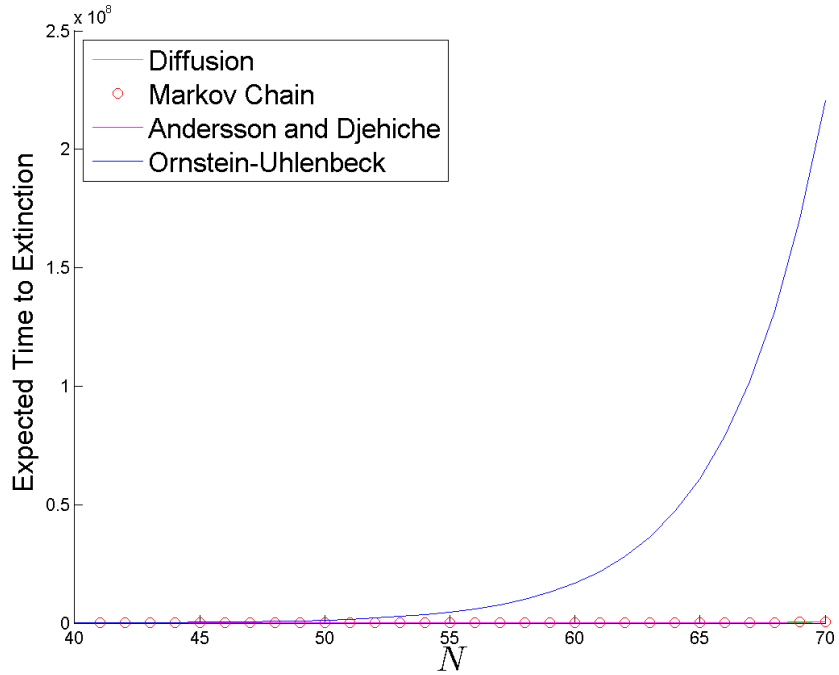

Figure 8: Expected time to extinction from quasi-stationarity for the SIS model, with approximations. $\beta = 2$, $\gamma = 1$, $N \in [40, 70]$.

In this series of Figures (6-8), the time to extinction from quasi-stationarity is considered. This is often considered a sensible starting point, as a disease that becomes the interest of a study has often already entrenched itself within a population. In these figures, the parameter N is varied, to allow for a variety of initial starting states, as each state considered is the quasi-stationary distribution for its respective parameter values. Figures (6-8) make use of equations (11), (12), (14) and (15). Note that as these graphs are reliant on a quasi-stationary state's existence, the parameter values considered must therefore all be $\mathbb{R}_0 > 1$.

In the case of $\beta = 1.2$, all approximations consistently overestimate time to extinction, however this effect is not present when considering β even greater than 1, such as in Figure (7). The Ornstein-Uhlenbeck approximation deviates greatly from the Markov process as both N and R_0 increase, culminating in Figure (8), where the Ornstein-Uhlenbeck approximation's expected time to extinction eclipses all others by a large margin. Accuracy of both diffusion and Andersson and Djehiche approximations improve greatly as R_0 increases (In relative difference but not in absolute). For values of R_0 closer to 1, the diffusion approximation outperforms the Andersson and Djehiche approximation, at least for small N, but this is not the case as R_0 increases. As before with the times to extinction from fixed initial states, the approximations predict greater time to extinction relative to the Markov chain for low R_0, and predict a lower time to extinction than the Markov Chain for higher R_0.

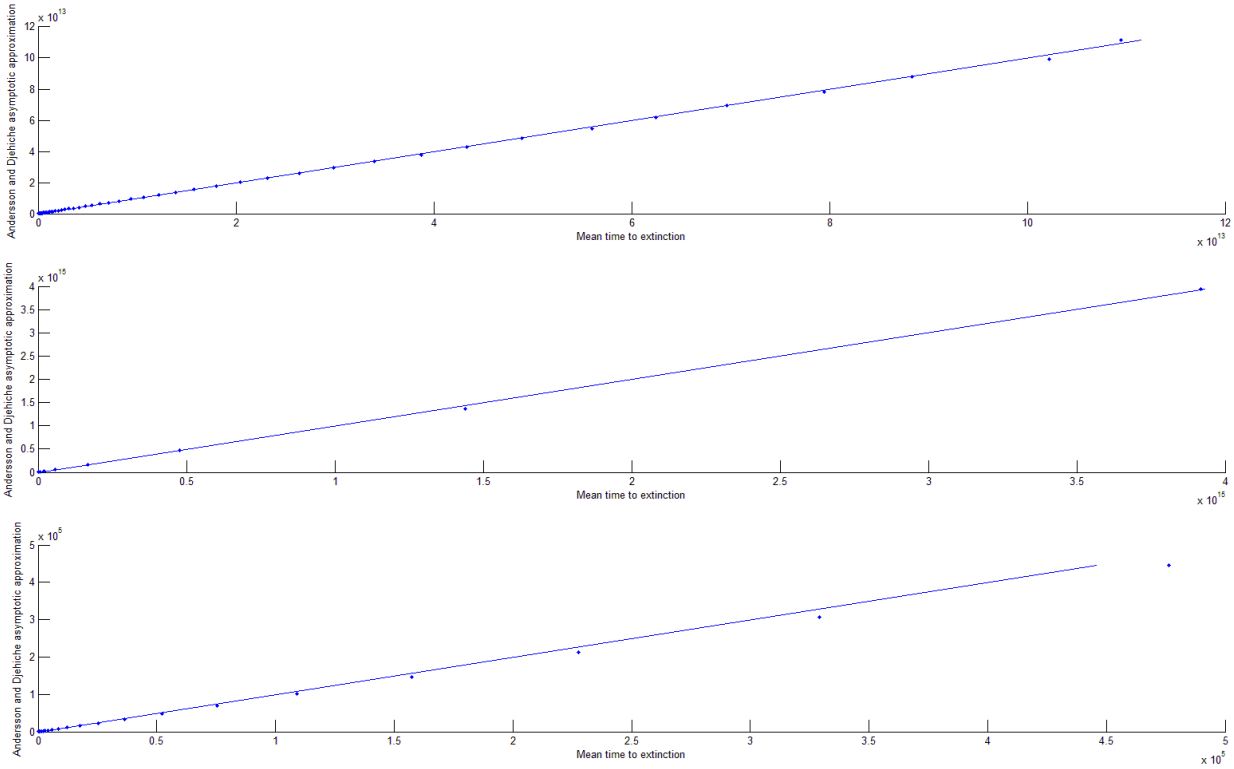

Figure 9: SIS model: expected time to extinction predicted by Andersson and Djehiche (1998)'s asymptotic approximation vs. expected time to extinction from quasi-stationarity, calculated by the eigenvalue method. $N = 20, \gamma = 1, \beta \in [2, 15]$. $N \in [20, 70], \gamma = 1, \beta = 2$ $N \in [20, 70], \gamma = 1, \beta = 3.5$. Line $y = x$ shown for comparison.

The approximation of Andersson and Djehiche (1998) was considered previously in Figures(5-7), and was found to approximate the time to extinction from a variety of initial states relatively well. The Figure (9) plots the mean time to extinction calculated via eigenvalue method against the approximation to better demostrate its goodness of fit. This figure makes use of equations (7) and (15).

The approximation of time to extinction derived by Andersson and Djehiche (1998), equation (15), received no numerical confirmation in the original paper, and was proven in a purely theoretical method. The figures 9 compare the approximation to the Markov process for numerical values, and show that the approximation is very good. Two of the figures match the like $x = y$ excellently, and the remaining line alsofitting well; there is a large absolute deviation from the line $x = y$, but small relative difference.

As the approximation was formulated under the assumption of large N, it is reassuring to discover that even for quite small values of N, the approximationl is accurate. Unfortunately, errors accumulating due to numerical approximation in the software prevents full analysis of larger values of N.

3.3 Coefficient of variation dependence

The coefficient of variation can be used to consider how far a disease process is from extinction. We consider the coefficient of variation of the Ornstein-Uhlenbeck approximation, and potential dependence of time to extinction upon it. The coefficient of variation is defined for any distribution as the ratio of the standard deviation σ to the mean μ:

$$CV = \frac{\sigma}{\mu}. \tag{36}$$

Note that this formula is only defined for non-zero mean, although this should be satisfied for the processes that we are considering.

The coefficient of variation has the following intuitive link to the time to extinction: as the variance increases, we are more likely to make a larger fluctuation about the endemic level, resulting in an extinction event. Therefore increasing variance should decrease expected time to extinction, and vice versa. A lower mean value decreases the amount of variability required to cause an extinction event. A decreasing mean should therefore decrease the time to extinction, and vice versa. A coefficient of variation that increases should therefore be the result of higher variance relative to mean level, and disease persistence should decrease as the coefficient of variation increases.

It is this intuitive link and the ease of calculability of the Coefficient of Variation that provides motivation for the study of this quantity relative to time to extinction. Formulae are derived for the time to extinction in terms of the Coefficient of Variation, and this relationship is studied with respect to a variety of expected parameter values, especially considering the parameter values taken as normal in previous studies.

To study dependence on coefficient of variation, we consider the Ornstein-Uhlenbeck process, that is the stationary Gaussian process which is used to approximate the limiting conditional distribution. The Ornstein-Uhlenbeck approximation of the quasi-stationary distribution is a normal approximation. This normal approximation provides an easy way to approximate this coefficient of variation by taking the coefficient of variation of the approximation instead of the true value.

3.3.1 SIS epidemic model

For the SIS model, the Ornstein-Uhlenbeck approximation of the quasi-stationary distribution is $N(Ni^*, N\sigma)$, where i^* and σ are the mean and variance respectively. We take the quasi-stationary distribution to be approximately normal, $I \sim N(Ni^*, N\sigma^2)$, where scaled mean $i^* = \dfrac{R_0 - 1}{R_0}$ and variance $\sigma^2 = \dfrac{1}{R_0}$, as shown in equations (2) and(10), it follows that the coefficient of variation is $CV = \dfrac{\sigma}{i^*\sqrt{N}}$. As this approximation is defined on $(-\infty, \infty)$, we consider the time to extinction as related to the chance of hitting a state equal to or below zero.

Rephrasing equation (11) to make the dependence on the coefficient of variation clearer, we obtain

$$\frac{CVi^*N\sqrt{2\pi}}{\gamma} \exp\left(\frac{1}{2CV^2}\right). \tag{37}$$

3.3.2 SIR epidemic model with demography

By considering the source of the Ornstein-Uhlenbeck approximation for the SIR model with demography, further simplification of the approximation can be made. Taking the quasi-stationary distribution to be approximately normal, $I \sim N(Ni^*, N\sigma^2)$, where scaled mean $i^* = \dfrac{R_0 - 1}{\alpha R_0}$ and variance $\sigma^2 = \dfrac{\left(R_0 - 1 + \frac{\mu}{\gamma+\mu}R_0^2\right)}{R_0^2}$, it follows that the coefficient of variation is $CV = \dfrac{\sigma}{i^*\sqrt{N}}$.

The probability of being in state $I = 1$ is approximated as stated in equation(32). Therefore, expected time to extinction is approximated as

$$\begin{aligned} E[\tau] &\approx \frac{\sigma\sqrt{2\pi N}}{\gamma} \exp\left(\frac{1}{2}\left(\frac{Ni^* - 1}{\sigma\sqrt{N}}\right)^2\right) \\ &\approx \frac{\sigma\sqrt{2\pi N}}{\gamma} \exp\left(\frac{1}{2}\left(\frac{Ni^*}{\sigma\sqrt{N}}\right)^2\right) \\ &= \frac{CVi^*N\sqrt{2\pi}}{\gamma} \exp\left(\frac{1}{2CV^2}\right). \end{aligned} \tag{38}$$

This approximation demonstrates the exponential relationship between coefficient of variation and time to extinction, in this case in the form of a dependence on $\exp\left(\frac{1}{2CV^2}\right)$

To understand how good an approximation this is, the results of the formula (38) are plotted against

mean simulated time to extinction. These initial parameter values were chosen as similar to those of Andersson and Britton (2000). The time to extinction is not also calculated using the eigenvalue method, due to the impact of increasing N causing a large increase in the necessary size of truncation, resulting in greater time for calculations.

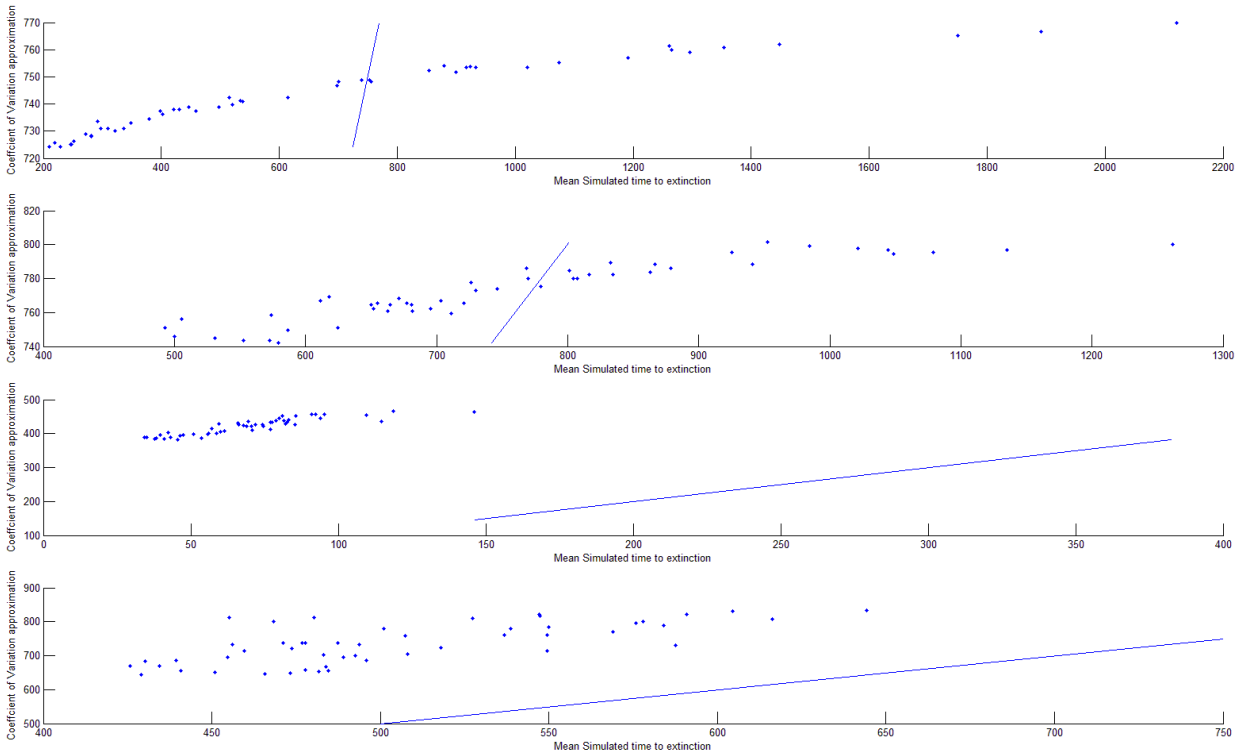

Figure 10: SIR model with demography, a parameter is varied, and formula (38) is plotted against mean simulated time to extinction, starting from deterministic equilibrium. In subfigure 1, parameter values are $N \in (300:350), R_0 = 10, \alpha = 40, \gamma = 0.2$. In subfigure 2, parameter values are $N \in (100:150), R_0 = 10, \alpha = 40, \gamma = 0.2$. In subfigure 3, parameter values are $N = 300, R_0 \in (8:12), \alpha = 30, \gamma = 0.2$. In subfigure 4, parameter values are $N = 300, R_0 = 10, \alpha \in (30:50), \mu = 0.2$. Each point represents the average of 200 simulations. The line $y = x$ is shown for comparison.

In each of the subfigures in Figure(10), different parameters are varied, to confirm that the dependence of the formula on each parameter is equivalent to that of simulation.

Whilst each of the subfigures shows a monotonically increasing trend, none show equality to the like $x = y$. There remains a disagreement in tersm of scale for all parameters considered. In the third subfigure of figure 10, R_0 is varied, and the linear trend remains strong, however there is a scale

discrepancy. Varying R_0 also produces the largest amount of variability. This is because varying R_0 has the greatest impact on extinction time, as it can result in both an extinction where a great number of individuals are initially infected, or a prolonged persistence time as the disease continues to replenish itself.

In the fourth subfigure of figure 10, α is varied, and whilst the formula (38) values produced are similar to that of the mean simulated time to extinction, this shows a large non-linear concave dependence, but are still monotonically increasing.

As the distribution moves away from the interference about the state $I = 0$, the reduction in distortion causes the formula (38) to better approximate the time to extinction. In the subfigures of Figure(10), values of N have been taken which reduce this distortion, allowing for a more normal representation of the quasi-stationary distribution of infectives. For lower values of N, the approximation does not appear similar to time to extinction, although it does still increase monotonically.

The approximation of formula (38) may be considered useful due to its quick speed of calculation, but appears to be flawed in terms of accuracy for the parameter values considered here.

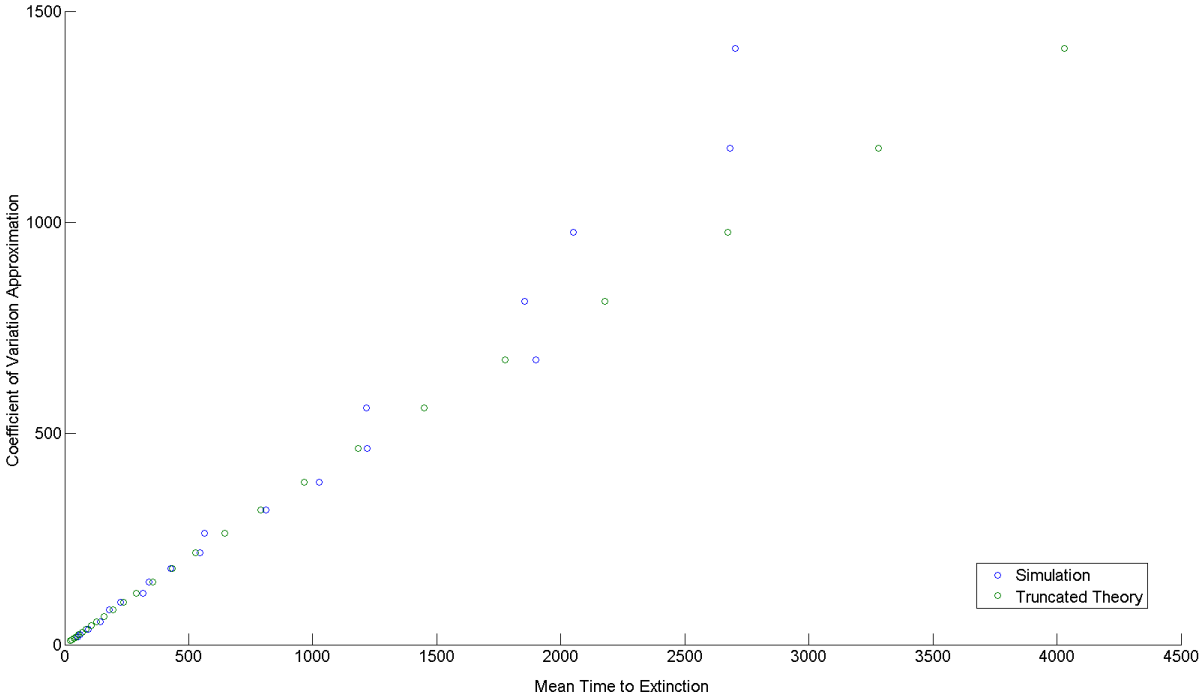

Figure 11: SIR model with demography, relationship between formula (38) and mean time to extinction from quasi-stationarity. For parameter values of van Herwaarden and Grasman: $R_0 = 2, \alpha = 2, \gamma = 0.2, N = [94 : 114]$. Time to extinction is calculated using a truncated state space $S_{max} = I_{max} = 200$, an adequate truncation consistent with larger values, with $S^* \in (10, 60)$ and $I^* \in (10, 60)$. Simulation started from deterministic equilibrium.

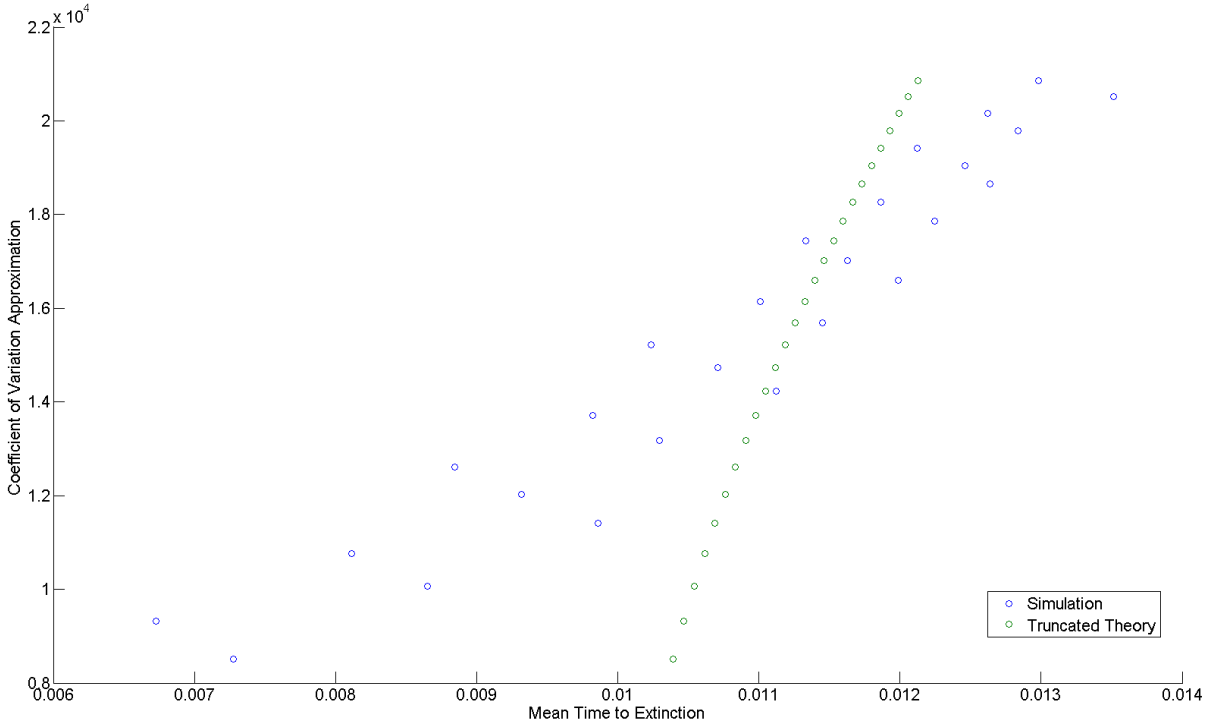

Figure 12: SIR model with demography, relationship between formula (38) and mean time to extinction. For parameter values of Nåsell: $R_0 = 10, \alpha = 500, \gamma = 0.2, N = [94 : 114]$.

Figures 11 and 12 both show the mean time to extinction continue its monotonic relationship, however there are large amounts of disagreement in scale.

For comparison with the values of van Herwaarden and Grasman, the values of N in figure 11 are lower than that used by Nåsell, and at these values the theoretical and simualtion results disagree, due to small N values, which skew the initial conditions (the deterministic equilibrium state) to a state unrepresentative of the true quasi-stationary distribution. The low values of N also aid the calculation of the time to extinction by eigenvalue method by reducing the size of the necessary truncation. Whilst figure 11 shows good agreement between these simulation and eigenvalue methods, in figure 12, where the parameters in Nåsell (1995) are used, the approximation disagrees with insufficient burn-in time to account for wildly varying initial conditions, that is the endemic equilibrium solution for the particular parameter values. For the parameter values considered, there is a linear relationship between formula (38) and mean time to extinction, but it is not equivalent to $x = y$.

3.3.3 Normality as the governing factor

As mentioned earlier, the approximation fails for low values of N to reach any level of acceptable approximation. This is because of the distortion of the quasi-stationary distribution that occurs near the origin. The formula (38) requires the quasi-stationary distribution to be approximately normal.

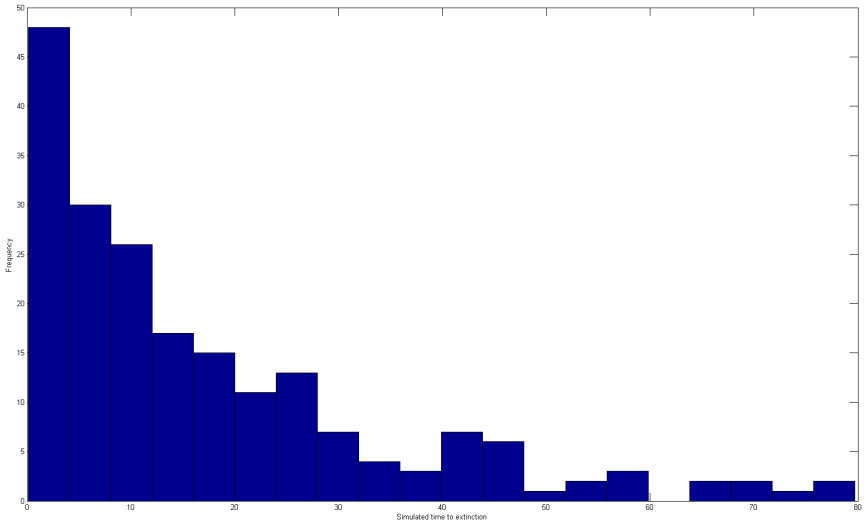

Figure 13: Simulated quasi-stationary distribution of the SIR model with demography, for $N = 90$. Note how it is non-normal - this is true for the parameter values of all points plotted in figure 12. Parameter values $R_0 = 10, \alpha = 40, \gamma = 0.2$, 240 simulations.

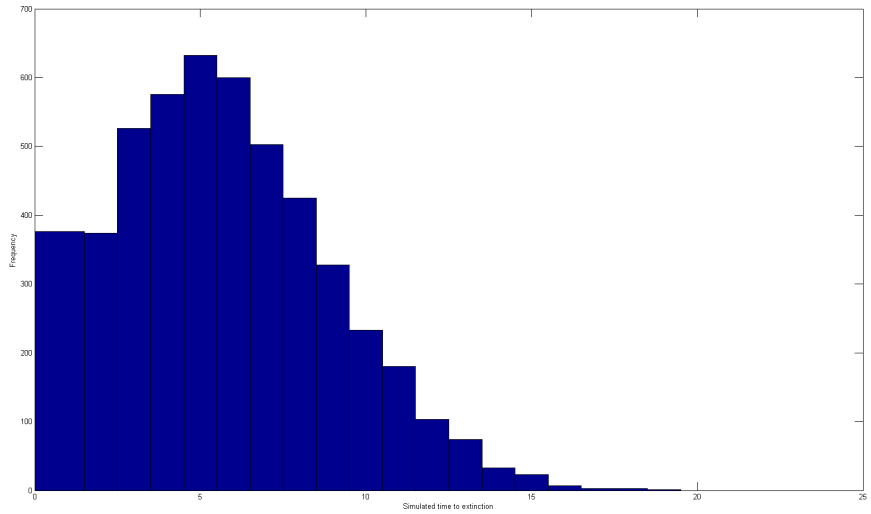

Figure 14: Simulated quasi-stationary distribution of the SIR model with demography, for the parameter values $N = 240, R_0 = 10, \alpha = 40, \gamma = 0.2$

Figure 14 represents a typical distribution from the previous simulated time to extinction, for a given set of parameters. The formula (38) is based on a normal approximation, and the distribution pictured is distinctly skewed. However, despite this dissimilarity, the trends in figures 11 and 12 are still strongly linear. As N increases, the approximation improves, as the normality of the distribution improves. This is demonstrated in comparisons between figures 13 and 14.

It is clear that the accuracy of approximation of the mean time to extinction using a Gaussian distribution is dependent on the normality of the quasi-stationary distribution. Accuracy of any further approximation is heavily reliant on the limiting conditional distribution already meeting minimum requirements for a measure of normality. The most important factor for considering the normality of a distribution for the purposes of this approximation is the likely asymmetry, particularly with regards to the left tail. Two methods of assessing this are the Jarque-Bera test (Thadewald,T. and Buning, H., 2004)and the condition $CV < \frac{1}{3}$.

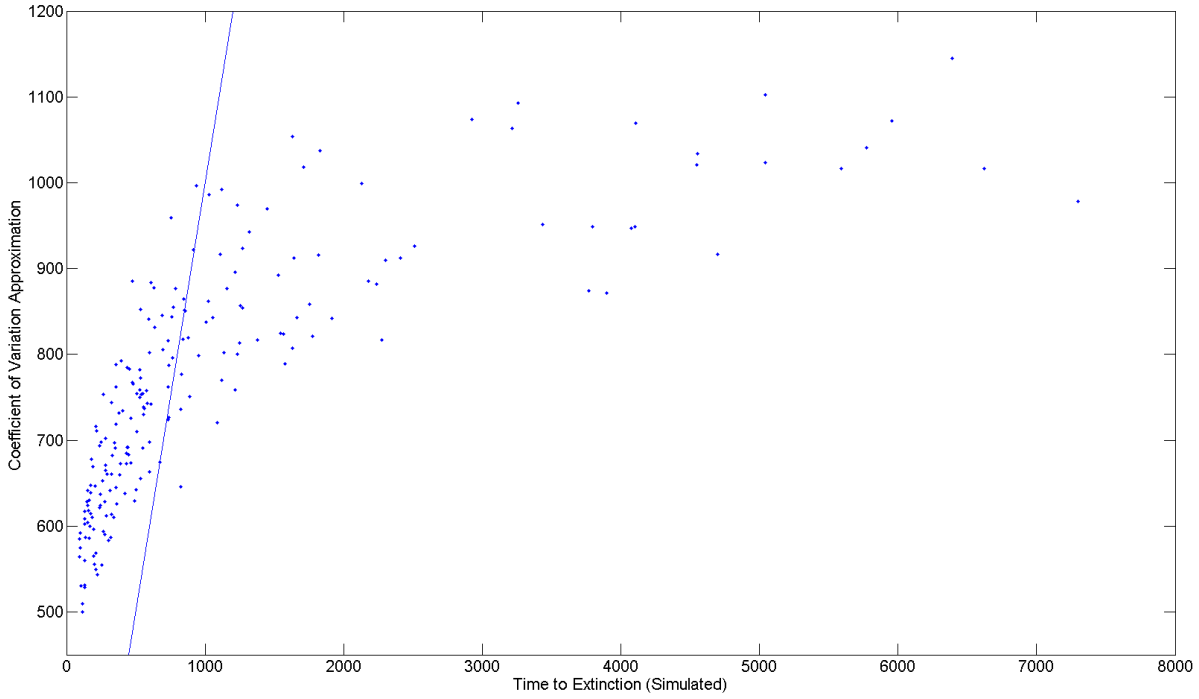

Figure 15: SIR model with demography, All parameters are varied, and formula (38) is plotted against mean simulated time to extinction, starting from deterministic equilibrium. Parameter values $N \in (250, 350), R_0 \in (8, 12), \alpha \in (35, 45), \gamma \in (0.15, 0.25)$. The line $x = y$ is also shown, representing the ideal approximation.

In figure 15, all combinations of parameter values within stated ranges are randomised, to compare a variety of times to extinction resulting from differing parameter values. Figure 15 demonstrates that the approximation is not fully valid for all possible parameter values, although it is in general increasing. Values which fall underneath the line are approximated perfectly by the formula(38), with all others under or overestimating. Some of these deviations from the line can be quite large.

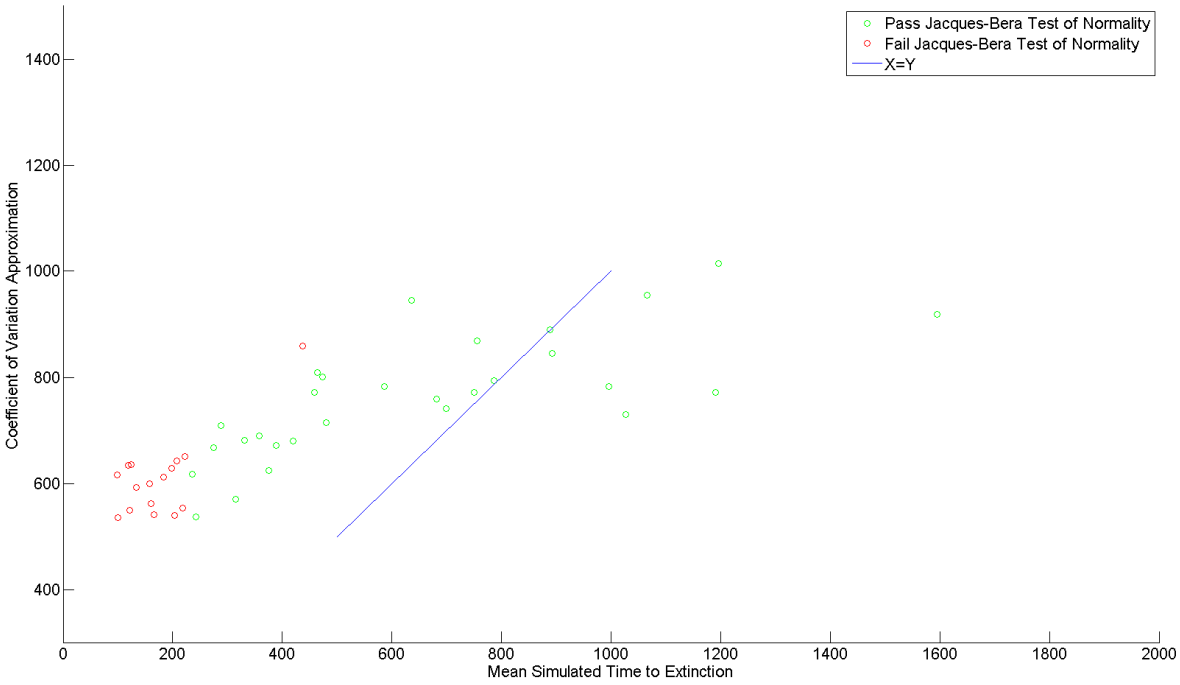

Figure 16: SIR model with demography, All parameters are varied, and formula(38) is plotted against mean simulated time to extinction, starting from deterministic equilibrium. Parameter values $N \in (250, 350), R_0 \in (8, 12), \alpha \in (35, 45), \gamma \in (0.15, 0.25)$. The line $x = y$ is also shown, representing the ideal approximation.

The formula(38) is derived from the assumption that the quasi-stationary distribution can be approximated by a normal distribution, so in figure 16 a quasi-stationary distribution has also been simulated for each parameter value combination resulting in a point. Points which meet criteria for normality are coloured green, whilst those which fail are coloured red. The parameter space used in this diagram is identical to that of figure 15. The test used is the Jarque-Bera test for normality, which compares the expected skewness and kurtosis with the simulated values. As the number of samples increases in the simulation, the probability that the test will reject the distribution increases, making this test at best a

rough guide. However, it does demonstrate a distinct trend.

The parameter values for the points which are red do not produce a sufficiently normal quasi-stationary distribution, and so the approximation is inaccurate. These cases are largely due to low values of N where the distribution does not become fully normal due to the extinction at $I = 0$, as shown in figure 14, forcing the distribution to skew. There are still several green points pictured in the far right of the diagram which deviate significantly from the line $x = y$, where the distribution is normal, but the time to extinction is far greater than the formula would suggest. These distributions typically have large spread and therefore, for low numbers of simulations, will produce a lower than representative fraction of extinctions. That is, increasing the number of simulations per point reduces the incidence of these points.

Note the two red points to the right of the line $x = y$. Again this results from parameter values causing a large spread, such as R_0 very large, in this case $R_0 = 12$. The test rejects normality in this case. This can again be remedied by increasing the number of simulations per point.

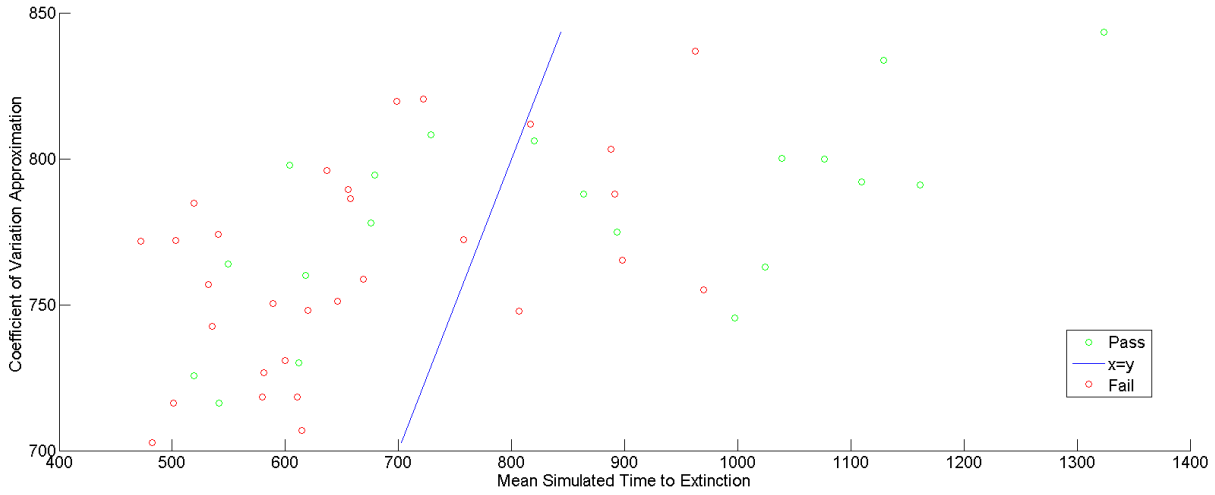

Figure 17: SIR model with demography, All parameters are varied, and formula(38) is plotted against mean simulated time to extinction, starting from deterministic equilibrium. Parameter values $N \in (250, 350), R_0 \in (8, 12), \alpha \in (35, 45), \gamma \in (0.15, 0.25)$. The line $x = y$ is also shown, representing the ideal approximation.

This figure measures normality by considering whether the Coefficient of Variation being less than a third (which are labelled 'Pass'). Here the trend does not agree, more non-normal results do not cluster

away from the line. This test is cruder, but far more transparent.

These diagrams demonstrate that the relationship with Coefficient of Variation is indeed increasing, but in a non-linear fashion. Earlier figures appear linear, despite the overall trend of non-linearity due to the choices of parameters. The Jarque-Bera test appears to be far more effective at identifying parameter values which produce non-normal distributions, as figure (17) does not demonstrate the same relationship between normal distribution producing parameter values and closeness to the line $x = y$.

4 SIS epidemic model without demography, with Erlang distributed infectious periods

The basic SIS model without demography is one of the most basic disease models studied, and has many features of real diseases that are useful for study. It is limited in its accuracy of real world behaviour as a result, although as seen in the previous section, trading accuracy for speed of calculation can often be a desired function. A common method of improving models is by adding a single complication and considering the ways in which it varies from the more basic model, allowing the features of the change to be most evident.

It is suggested by Lloyd (2000) that the disease persistence is decreased for models with Erlang-distributed infectious periods relative to other parameters and therefore quantities of interest, leading to a more realistic distribution of time to extinction. Whilst Lloyd's work is focussed on deterministic approximations of this amended model, the stochastic equivalent has received little study. This section therefore aims to consider how the stochastic SIS epidemic model without demography is changed when Erlang-distributed infectious periods are included, as well as studying adapted versions of previously considered approximations of the SIS model without demography.

4.1 Model formulation

Here we consider the SIS model, chosen for its simplicity, and modify it to include an Erlang distributed infectious period. This model is chosen for comparison as many of the results for the non-Erlang case are already known. The model contains no immunity, with a fixed population of size N, consisting at time t of $S(t)$ susceptible individuals, and $I(t)$ infectious individuals, such that $N = S(t) + I(t)$. Infectious individuals pass through k substages $I_1(t), I_2(t), ..., I_k(t)$ in order, with $\sum_{m=1}^{k} I_m(t) = I(t)$. The total infectious period thus follows an Erlang distribution. The transition rates for this model are as follows.

Event	State transition	Transition rate
Infection of susceptible	$(S, I_1) \to (S-1, I_1+1)$	$\frac{\beta}{N}\left(N - \sum_{m=1}^{k} I_m\right)\left(\sum_{m=1}^{k} I_m\right)$
Transition to next infectious substage	$(I_m, I_{m+1}) \to (I_m - 1, I_{m+1}+1)$	$k\gamma I_m$ $(m = 1, ..., k-1)$
Recovery of infected	$(S, I_k) \to (S+1, I_k - 1)$	$k\gamma I_k$

This results in a basic reproduction number $R_0 = \beta/\gamma$, as before. The total infectious period has mean $1/\gamma$, variance $1/k\gamma^2$, giving flexibility to vary the spread while keeping the mean fixed. Note that for $k = 1$, the model reduces to the basic SIS model.

The Erlang distribution is not memoryless, so when considering fixed initial states we assume that all infectives start in the first infectious substage. However, studying an entrenched disease the quasi-stationary distribution contains infectives in all substages.

As this is once again a closed population model, $N = S(t) + \Sigma_{m=1}^{k} I_m(t)$, allowing for one of the $k+1$ states to be removed from the model. Here, we again choose S, to allow for easier calculation of the sum of infectives at any time.

4.2 Deterministic model

We again scale the model to allow for deterministic approximation, assuming that the scaled discrete process is adequately approximated by a continuous process. We take $\frac{1}{N}S(t) = s(t)$ and $\frac{1}{N}I_m(t) = i_m(t)$. The equations for the deterministic approximation are as follows.

$$\frac{di_1}{dt} = \beta\left(1 - \sum_{m=1}^{k} i_m\right)\left(\sum_{m=1}^{k} i_m\right) - k\gamma i_1,$$
$$\frac{di_m}{dt} = k\gamma i_{m-1} - k\gamma i_m \qquad m = 2, ..., k.$$

This system has two equilibria, as before. There remains a fully extinct equilibrium, and an endemic equilibrium $i_m^* = \frac{1}{k}\left(1 - \frac{\gamma}{\beta}\right)$, $m = 1, ..., k$.

For given values of k, the deterministic approximation can be solved numerically for time to extinction assuming $R_0 < 1$, as before in the case of $k = 1$. Applying initial conditions to the equations, time to reach the case of $\max\{I_1, I_2, \ldots, I_k\} < 0.5$ can be calculated. The continuity correction is required to allow for a finite time to extinction. As before, for values of $R_0 > 1$, the time to extinction remains infinite.

4.3 Stochastic model

4.3.1 Diffusion approximation

As before, the model may be approximated by a (multivariate) diffusion process $\boldsymbol{X}(t)$ satisfying

$$\begin{aligned} dX_1 &= \left(\frac{\beta}{N}\left(\sum_i X_i\right)\left(N - \sum_i X_i\right) - k\gamma X_1\right) dt + \left(\sqrt{\frac{\beta}{N}\left(\sum_i X_i\right)\left(N - \sum_i X_i\right) + k\gamma X_1}\right) dW_1, \\ dX_j &= \left(k\gamma X_{j-1} - k\gamma X_j\right) dt + \left(\sqrt{k\gamma X_{j-1} + k\gamma X_j}\right) dW_j \text{ for } j = 2, ..., k, \end{aligned} \tag{39}$$

where $W_1(t), W_2(t), ..., W_k(t)$ are independent standard Brownian motions.

The mean time to extinction $T^D(\boldsymbol{x})$ satisfies the Kolmogorov backward equation

$$\begin{aligned} &\left(\frac{\beta}{N}\left(N - \sum_{i=1}^k X_i\right)\left(\sum_{i=1}^k X_i\right) - k\gamma X_1\right)\frac{\partial T^D}{\partial X_1} + \sum_{j=2}^k \left(k\gamma X_{j-1} - k\gamma X_j\right)\frac{\partial T^D}{\partial X_j} \\ &+ \frac{1}{2}\left(\left(\frac{\beta}{N}\left(N - \sum_{i=1}^k X_i\right)\left(\sum_{i=1}^k X_i\right) + k\gamma X_1\right)\frac{\partial^2 T^D}{\partial X_1^2} + \sum_{j=2}^k \left(k\gamma X_{j-1} + k\gamma X_j\right)\frac{\partial^2 T^D}{\partial X_j^2} - \sum_{j=2}^k \left(k\gamma X_{j-1}\right)\frac{\partial^2 T^D}{\partial X_{j-1}\partial X_j}\right) \\ &= -1, \end{aligned}$$

with boundary conditions $T^D(\mathbf{0}) = 0$, $\left.\frac{\partial T^D}{\partial X_i}\right|_{X_i=0} = 0$ $(i = 1, 2, \ldots, k)$ and $\sum_i \left.\frac{\partial T^D}{\partial X_i}\right|_{\sum_{i=1}^k X_i = N} = 0$ $(i = 1, 2, \ldots, k)$. (Gardiner, 2009, section 6.6.1)

4.3.2 Ornstein-Uhlenbeck approximation

We can again further approximate the process by a (multivariate) Ornstein-Uhlenbeck process $\widetilde{X}(t)$, where $\widetilde{X}(t)$ is the solution to

$$d\widetilde{X} = B(\widetilde{X}(t) - N\boldsymbol{i}^*)dt + SdW$$

where B is the local drift matrix, $\boldsymbol{i}^*$ is the deterministic equilibrium, and S is the local variance matrix. The quasi-stationary distribution can be approximated by a multivariate Gaussian distribution with mean $N\boldsymbol{i}^*$ and variance matrix Σ satisfying

$$B\Sigma + \Sigma B^T = -S.$$

The model has been scaled by a factor of N for convenience, so that in equilibrium, $i_m^* = \frac{1}{k}\left(1 - \frac{\gamma}{\beta}\right)$, $\sum_{m=1}^{k} i_m^* = 1 - \frac{\gamma}{\beta}$. The local drift matrix at endemic equilibrium is

$$B = \begin{pmatrix} \beta - 2\beta\sum\limits_k i_m^* - k\gamma & \beta - 2\beta\sum\limits_k i_m^* & \beta - 2\beta\sum\limits_k i_m^* & \cdots & \beta - 2\beta\sum\limits_k i_m^* \\ k\gamma & -k\gamma & 0 & \cdots & 0 \\ 0 & k\gamma & -k\gamma & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & 0 \\ 0 & 0 & 0 & k\gamma & -k\gamma \end{pmatrix}$$

$$= \begin{pmatrix} (2-k)\gamma - \beta & 2\gamma - \beta & 2\gamma - \beta & \cdots & 2\gamma - \beta \\ k\gamma & -k\gamma & 0 & \cdots & 0 \\ 0 & k\gamma & -k\gamma & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & 0 \\ 0 & 0 & 0 & k\gamma & -k\gamma \end{pmatrix}.$$

While the local variance matrix is

$$S = \begin{pmatrix} \beta(1-\sum_k i_j^*) + k\gamma i_1^* & -k\gamma i_1^* & 0 & \cdots & 0 \\ -k\gamma i_1^* & k\gamma(i_1^* + i_2^*) & -k\gamma i_2^* & \cdots & 0 \\ 0 & -k\gamma i_2^* & k\gamma(i_2^* + i_3^*) & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & -k\gamma i_{k-1}^* \\ 0 & 0 & 0 & -k\gamma i_{k-1}^* & k\gamma(i_{k-1}^* + i_k^*) \end{pmatrix}$$

$$= \begin{pmatrix} \gamma + \gamma(1-\frac{\gamma}{\beta}) & \gamma(1-\frac{\gamma}{\beta}) & 0 & \cdots & 0 \\ -\gamma(1-\frac{\gamma}{\beta}) & 2\gamma(1-\frac{\gamma}{\beta}) & -\gamma(1-\frac{\gamma}{\beta}) & \cdots & 0 \\ 0 & -\gamma(1-\frac{\gamma}{\beta}) & 2\gamma(1-\frac{\gamma}{\beta}) & \cdots & 0 \\ \vdots & \vdots & \vdots & \ddots & -\gamma(1-\frac{\gamma}{\beta}) \\ 0 & 0 & 0 & -\gamma(1-\frac{\gamma}{\beta}) & 2\gamma(1-\frac{\gamma}{\beta}) \end{pmatrix}.$$

From here, the solution to the matrix equation was guessed, by considering numerical values of $k = 2, 3$ and checked by multiplication following simplification. The equation $\sum_{j=1}^{k} \left(B_{a,j}\sigma_{j,b} + \sigma_{a,j}(B_{j,b})^T\right) = -S_{a,b}$ is equivalent to $B\sigma + \sigma B^T = -S$ provided it holds for all a, b. Additionally, the matrix σ is symmetric, $\sigma_{a,b} = \sigma_{b,a}$ and $B_{a,b} = B_{b,a}^T$, Therefore $2\sum_{j=1}^{k} B_{a,j}\sigma_{j,a} = -S_{a,a}$

On the diagonal, in the case: $a = b = 1$ we have

$$2\sum_{j=1}^{k} B_{a,j}\sigma_{j,a} = 2\left((k\gamma)\left(\frac{2\gamma}{\beta} - 1\right) + \sum_{j=2}^{k}(2\gamma - \beta)\left(\frac{2\gamma}{\beta} - 1\right)\right) = \gamma + \gamma\left(1 - \frac{\gamma}{\beta}\right) = -S_{1,1}.$$

On the diagonal, the case $a = b = 2, 3, .., k$ we have

$$2\sum_{j=1}^{k} B_{a,j}\sigma_{j,a} = 2\left((k\gamma)\left(\frac{2\gamma}{\beta} - 1\right) + (-k\gamma)\left(k - 1 - \frac{\gamma(k-2)}{\beta}\right)\right) = 2k\gamma - \frac{2k\gamma^2}{\beta} = -S_{a,a}.$$

In the case of entries adjacent to the main diagonal ($a = 1, b = 2$) and ($a = 2, b = 1$),

$$\begin{aligned}\sum_{j=1}^{k}\left(B_{a,j}\sigma_{j,b} + \sigma_{a,j}B_{j,b}^{T}\right) =& \frac{1}{k^2}\left((k\gamma)\left(k-1-\frac{\gamma(k-2)}{\beta}\right)+\left(-k\gamma\left(\frac{2\gamma}{\beta}-1\right)\right)+\left(\left(\beta-2\beta\left(1-\frac{\gamma}{\beta}\right)-k\gamma\right)\left(\frac{2\gamma}{\beta}-1\right)\right.\right.\\ &\left.\left.+(\beta-2\beta\left(1-\frac{\gamma}{\beta}\right)\right)\left(k-1-\frac{\gamma(k-2)}{\beta}\right)+\sum_{j=3}^{k}\left(\left(\frac{2\gamma}{\beta}-1\right)\left(\beta-2\beta\left(1-\frac{\gamma}{\beta}\right)\right)\right)\right)\\ =& -k\gamma\left(1-\frac{\gamma}{\beta}\right) = -S_{a,b}.\end{aligned}$$

In the case of entries adjacent to the main diagonal ($a = 2, 3, ..., k, b = a-1$) and ($a = 3, 4, ...k-1, b = a-1$),

$$\sum_{j=1}^{k}\left(B_{a,j}\sigma_{j,b} + \sigma_{a,j}B_{j,b}^{T}\right) = \frac{1}{k^2}\left((k\gamma)\left(k-1-\frac{\gamma(k-2)}{\beta}\right)+(-k\gamma)\left(\frac{2\gamma}{\beta}-1\right)\right) = -k\gamma\left(1-\frac{\gamma}{\beta}\right) = -S_{a,b}.$$

In the case of entries ($a = 1, b = 3, 4, ..., k$) and ($a = 3, 4, ..., k., b = 1$),

$$\begin{aligned}\sum_{j=1}^{k}\left(B_{a,j}\sigma_{j,b} + \sigma_{a,j}B_{j,b}^{T}\right) =& \frac{1}{k^2}\left(k-1-\frac{\gamma(k-2)}{\beta}\right)\left(\beta-2\beta\left(1-\frac{\gamma}{\beta}\right)\right)+\left(\frac{2\gamma}{\beta}-1\right)\left(\beta-2\beta\left(1-\frac{\gamma}{\beta}\right)-k\gamma\right)\\ &+\sum_{k-2}\left(\frac{2\gamma}{\beta}-1\right)\left(\beta-2\beta\left(1-\frac{\gamma}{\beta}\right)\right) = 0 = -S_{a,b}.\end{aligned}$$

In the case of all other entries,

$$\sum_{j=1}^{k}\left(B_{a,j}\sigma_{j,b} + \sigma_{a,j}B_{j,b}^{T}\right) = 2\left((k\gamma)\left(\frac{2\gamma}{\beta}-1\right)+(-k\gamma)\left(\frac{2\gamma}{\beta}-1\right)\right) = 0 = -S_{a,b}.$$

Therefore, the stationary process of the Ornstein-Uhlenbeck distribution approximation has mean $\mu_i^* = \frac{1}{k}\left(1-\frac{1}{R_0}\right)$, $\forall i = 1, 2, \ldots, k$, and variance matrix Σ with entries

$$\sigma_{pq} = \begin{cases}\frac{1}{k^2}\left((k-1)-\frac{(k-2)}{R_0}\right) & p = q,\\ \frac{1}{k^2}\left(\frac{2}{R_0}-1\right) & p \neq q.\end{cases} \tag{40}$$

Here, the mean and covariance values are valid for any integer $k \geq 1$. This allows us to estimate time to extinction as before, by considering $P(I = 1)$ in quasi-stationarity, and taking the continuity correction $I_k \leq 0.5$, $I_j = 0\ \forall j \neq k$. Note that all diagonal and nondiagonal entries have the same form, and that $\text{Var}[I] = \sum_{p,q}\sigma_{pq} = \frac{1}{R_0}$, that is to say it does not vary with respect to k. This suggests that the

mean time to extinction does not depend on k.

4.3.2.1 Partial Differential Equation

Consider a diffusion approximation evolving in region Ω with boundary $S = S_a \cup S_r$, absorption at S_a and reflection at S_r. In Section 6.6. of Gardiner(2009), it is established that, correcting for the typo in equation (6.6.8), factor 2 should be $\frac{1}{2}$) that, with $T(\boldsymbol{x})$ denoting expected time to absorption in boundary segment S_a from state x then

$$\sum_i A_i(\boldsymbol{x}) \frac{\partial T(\boldsymbol{x})}{\partial x_i} + \frac{1}{2} \sum_{i,j} B_{ij}(\boldsymbol{x}) \frac{\partial^2 T}{\partial x_i \partial x_j} = -1 \text{ in } \Omega$$

subject to boundary conditions (6.6.15-6.6.16)

$$T(\boldsymbol{x}) = 0 \text{ on } S_a, \tag{41}$$

$$\sum_{i,j} n_i B_{ij} \frac{\partial T(\boldsymbol{x})}{\partial x_j} = 0 \text{ on } S_r, \tag{42}$$

where $\boldsymbol{n}$ is the normal vector to the boundary S_r.

4.3.2.2 Finite Element Method

For Finite Element Method, variational formulation is given by (JN Reddy (2006), An introduction to the Finite Element Method, 3rd edition)

$$\int_\Omega \left(\sum_i A_i(\boldsymbol{x}) \frac{\partial T(\boldsymbol{x})}{\partial x_i} + \frac{1}{2} \sum B_{ij}(\boldsymbol{x}) \frac{\partial^2 T}{\partial x_i \partial x_j} \right) w(\boldsymbol{x}) d\Omega = -\int_\Omega w(\boldsymbol{x}) d\Omega$$

for appropriate test functions $w(\boldsymbol{x})$ defined on Ω.

Second order terms must be integrated by parts. Treating x_i, x_j symmetrically, and denoting by $\hat{\boldsymbol{n}}$ the outward unit normal vector to S, then

$$\int_\Omega w(\boldsymbol{x}) B_{ij}(\boldsymbol{x}) \frac{\partial^2 T}{\partial x_i \partial x_j} d\Omega = \frac{1}{2} \int_S w(\boldsymbol{x}) B_{ij}(\boldsymbol{x}) \left(\frac{\partial T}{\partial x_i} \hat{n}_i + \frac{\partial T}{\partial x_j} \frac{1}{2} \int_\Omega w(\boldsymbol{x}) B_{ij}(\boldsymbol{x}) \left(\frac{\partial T}{\partial x_i} \frac{\partial (w B_{ij})}{\partial x_j} + \frac{\partial T}{\partial x_j} \frac{\partial (w B_{ij})}{\partial x_i} \right) d\Omega \right.$$

Boundary terms:

On S_r, noting that variance matrix $B(\boldsymbol{x})$ is symmetric, we have

$$\int_{S_r} w(\boldsymbol{x}) \sum_{i,j} B_{ij}(\boldsymbol{x}) \left(\frac{\partial T}{\partial x_i} \hat{n_j} + \frac{\partial T}{\partial x_j} \hat{n_i} \right) dS = \int_{S_r} w(\boldsymbol{x}) \left(\sum_{i,j} \hat{n_i} B_{ij}(\boldsymbol{x}) \frac{\partial T}{\partial x_j} + \sum_{i,j} \hat{n_j} B_{ji}(\boldsymbol{x}) \frac{\partial T}{\partial x_i} \right) dS = 0+0, \text{ from 42.}$$

On S_a, the condition $T(\boldsymbol{x}) = 0$ implies that test functions satisfy $w(\boldsymbol{x}) = 0$, so again boundary contribution is zero.

Hence we have

$$\begin{aligned}
&\int_\Omega w(\boldsymbol{x}) B_{ij} \frac{\partial^2 T}{\partial x_i \partial x_j} d\Omega \\
&\qquad = -\frac{1}{2} \int_\Omega \left(\frac{\partial T}{\partial x_i} \frac{\partial (w B_{ij})}{\partial x_j} + \frac{\partial T}{\partial x_j} \frac{\partial (w B_{ij})}{\partial x_i} \right) d\Omega \\
&\qquad = -\frac{1}{2} \int_\Omega \left(\frac{\partial T}{\partial x_i} \left(B_{ij}(\boldsymbol{x}) \frac{\partial w}{\partial x_j} + w(\boldsymbol{x}) \frac{\partial B_{ij}}{\partial x_j} \right) + \frac{\partial T}{\partial x_j} \left(B_{ij}(\boldsymbol{x}) \frac{\partial w}{\partial x_i} + w(\boldsymbol{x}) \frac{\partial B_{ij}}{\partial x_i} \right) \right) d\Omega \\
&\qquad = -\frac{1}{2} \int_\Omega B_{ij}(\boldsymbol{x}) \left(\frac{\partial T}{\partial x_i} \frac{\partial w}{\partial x_j} + \frac{\partial T}{\partial x_j} \frac{\partial w}{\partial x_i} \right) + w(\boldsymbol{x}) \left(\frac{\partial B_{ij}}{\partial x_j} \frac{\partial T}{\partial x_i} + \frac{\partial B_{ij}}{\partial x_i} \frac{\partial T}{\partial x_j} \right) d\Omega
\end{aligned}$$

So the variational form of the PDE is

$$\begin{aligned}
&\int_\Omega \sum_i A_i(\boldsymbol{x}) w(\boldsymbol{x}) \frac{\partial T}{\partial x_i} d\Omega - \frac{1}{4} \int_\Omega \sum_{i,j} B_{ij}(\boldsymbol{x}) \left(\frac{\partial T}{\partial x_i} \frac{\partial w}{\partial x_j} + \frac{\partial T}{\partial x_j} \frac{\partial w}{\partial x_i} \right) d\Omega \\
&\qquad -\frac{1}{4} \int_\Omega \sum_{i,j} w(\boldsymbol{x}) \left(\frac{\partial B_{ij}}{\partial x_j} \frac{\partial T}{\partial x_i} + \frac{\partial B_{ij}}{\partial x_i} \frac{\partial T}{\partial x_j} \right) d\Omega = -\int_\Omega w(\boldsymbol{x}) d\Omega
\end{aligned}$$

with $T(\boldsymbol{x}) = 0$ on S_a.

However, variance matrix $B(\boldsymbol{x})$ is symmetric, therefore

$$\begin{aligned}
&\int_\Omega \sum_{i,j} w(\boldsymbol{x}) \left(\frac{\partial B_{ij}}{\partial x_j} \frac{\partial T}{\partial x_i} + \frac{\partial B_{ij}}{\partial x_i} \frac{\partial T}{\partial x_j} \right) d\Omega \\
&\quad = \int_\Omega 2 \sum_i w(\boldsymbol{x}) \frac{\partial B_{ii}}{\partial x_i} \frac{\partial T}{\partial x_i} + \sum_{i<j} w(\boldsymbol{x}) \left(\frac{\partial B_{ij}}{\partial x_j} \frac{\partial T}{\partial x_i} + \frac{\partial B_{ij}}{\partial x_i} \frac{\partial T}{\partial x_j} \right) + \sum_{i<j} w(\boldsymbol{x}) \left(\frac{\partial B_{ji}}{\partial x_i} \frac{\partial T}{\partial x_j} + \frac{\partial B_{ji}}{\partial x_j} \frac{\partial T}{\partial x_i} \right) d\Omega \\
&\quad = \int_\Omega 2 \sum_i w(\boldsymbol{x}) \frac{\partial B_{ii}}{\partial x_i} \frac{\partial T}{\partial x_i} + \sum_{i<j} w(\boldsymbol{x}) \left(\frac{\partial B_{ij}}{\partial x_j} \frac{\partial T}{\partial x_i} + \frac{\partial B_{ij}}{\partial x_i} \frac{\partial T}{\partial x_j} \right) + \sum_{i<j} w(\boldsymbol{x}) \left(\frac{\partial B_{ij}}{\partial x_i} \frac{\partial T}{\partial x_j} + \frac{\partial B_{ij}}{\partial x_j} \frac{\partial T}{\partial x_i} \right) d\Omega \\
&\quad = \int_\Omega 2 \sum_i w(\boldsymbol{x}) \frac{\partial B_{ii}}{\partial x_i} \frac{\partial T}{\partial x_i} + 2 \sum_{i<j} w(\boldsymbol{x}) \left(\frac{\partial B_{ij}}{\partial x_j} \frac{\partial T}{\partial x_i} + \frac{\partial B_{ij}}{\partial x_i} \frac{\partial T}{\partial x_j} \right) d\Omega.
\end{aligned}$$

Similarly,

$$\int_\Omega \sum_{i,j} B_{ij}(\boldsymbol{x})\left(\frac{\partial T}{\partial x_i}\frac{\partial w}{\partial x_j}+\frac{\partial T}{\partial x_j}\frac{\partial w}{\partial x_i}\right)d\Omega$$
$$=\int_\Omega 2\sum_i B_{ii}(\boldsymbol{x})\frac{\partial T}{\partial x_i}\frac{\partial w}{\partial x_i}+\sum_{i<j} B_{ij}(\boldsymbol{x})\left(\frac{\partial T}{\partial x_i}\frac{\partial w}{\partial x_j}+\frac{\partial T}{\partial x_j}\frac{\partial w}{\partial x_i}\right)+\sum_{i<j} B_{ji}(\boldsymbol{x})\left(\frac{\partial T}{\partial x_i}\frac{\partial w}{\partial x_i}+\frac{\partial T}{\partial x_i}\frac{\partial w}{\partial x_j}\right)d\Omega$$
$$=\int_\Omega 2\sum_i B_{ii}(\boldsymbol{x})\frac{\partial T}{\partial x_i}\frac{\partial w}{\partial x_i}+2\sum_{i<j} B_{ij}(\boldsymbol{x})\left(\frac{\partial T}{\partial x_i}\frac{\partial w}{\partial x_j}+\frac{\partial T}{\partial x_j}\frac{\partial w}{\partial x_i}\right)d\Omega.$$

Hence variational form of PDE becomes

$$\int_\Omega \sum_i A_i(\boldsymbol{x})w(\boldsymbol{x})\frac{\partial T}{\partial x_i}d\Omega-\frac{1}{2}\int_\Omega\left(\sum_i B_{ii}(\boldsymbol{x})\frac{\partial T}{\partial x_i}\frac{\partial w}{\partial x_i}+\sum_{i<j} B_{ij}(\boldsymbol{x})\left(\frac{\partial T}{\partial x_i}\frac{\partial w}{\partial x_j}+\frac{\partial T}{\partial x_j}\frac{\partial w}{\partial x_i}\right)\right)d\Omega$$
$$-\frac{1}{2}\int_\Omega\left(\sum_i w(\boldsymbol{x})\frac{\partial B_{ii}}{\partial x_i}\frac{\partial T}{\partial x_i}+\sum_{i<j} w(\boldsymbol{x})\left(\frac{\partial B_{ij}}{\partial x_j}\frac{\partial T}{\partial x_i}+\frac{\partial B_{ij}}{\partial x_i}\frac{\partial T}{\partial x_j}\right)\right)d\Omega=-\int_\Omega w(\boldsymbol{x})d\Omega$$

with $T(\boldsymbol{x})=0$ on S_a.

For 2-dimensional models, with $\boldsymbol{x}=(x,y)$, this reduces to

$$\int_\Omega\left(A_1(\boldsymbol{x})w(\boldsymbol{x})\frac{\partial T}{\partial x}+A_2(\boldsymbol{x})w(\boldsymbol{x})\frac{\partial T}{\partial y}\right)d\Omega$$
$$-\frac{1}{2}\int_\Omega\left(B_{11}(\boldsymbol{x})\frac{\partial T}{\partial x}\frac{\partial w}{\partial x}+B_{22}\frac{\partial T}{\partial y}\frac{\partial w}{\partial y}+B_{12}(\boldsymbol{x})\frac{\partial T}{\partial x}\frac{\partial w}{\partial y}+B_{12}(\boldsymbol{x})\frac{\partial T}{\partial y}\frac{\partial w}{\partial x}\right)d\Omega$$
$$-\frac{1}{2}\int_\Omega\left(w(\boldsymbol{x})\frac{\partial B_{11}}{\partial x}\frac{\partial T}{\partial x}+w(\boldsymbol{x})\frac{\partial B_{22}}{\partial y}\frac{\partial T}{\partial y}+w(\boldsymbol{x})\frac{\partial B_{12}}{\partial x}\frac{\partial T}{\partial y}+w(\boldsymbol{x})\frac{\partial B_{12}}{\partial y}\frac{\partial T}{\partial x}\right)d\Omega$$
$$+\int_\Omega w(\boldsymbol{x})d\Omega=0$$

with $T(\boldsymbol{x})=0$ on S_a.

Let x denote state 1 infectives, y denote stage 2 infectives. Then

$$A(x,y)=\begin{pmatrix}\frac{\beta}{N}(x+y)(N-x-y)-2\gamma x\\ 2\gamma x-2\gamma y\end{pmatrix},B(x,y)=\begin{pmatrix}\frac{\beta}{N}(x+y)(N-x-y)+2\gamma x & -2\gamma x\\ -2\gamma x & 2\gamma x+2\gamma y\end{pmatrix}$$

so variational form is

$$\begin{aligned}
&\int_\Omega \left(\left(\frac{\beta}{N}(x+y)(N-x-y) - 2\gamma x \right) w \frac{\partial T}{\partial x} + (2\gamma x - 2\gamma y) w \frac{\partial T}{\partial y} \right) d\Omega \\
-\frac{1}{2}\int_\Omega &\left(\left(\frac{\beta}{N}(x+y)(N-x-y) + 2\gamma x \right) \frac{\partial T}{\partial x}\frac{\partial w}{\partial x} + (2\gamma x + 2\gamma y)\frac{\partial T}{\partial x}\frac{\partial w}{\partial y} - 2\gamma x \frac{\partial T}{\partial x}\frac{\partial w}{\partial y} - 2\gamma x \frac{\partial T}{\partial y}\frac{\partial w}{\partial x} \right) d\Omega \\
-\frac{1}{2}\int_\Omega &\left(\left(\frac{\beta}{N}(N-2x-2y) + 2\gamma \right) w \frac{\partial T}{\partial x} + 2\gamma w \frac{\partial T}{\partial y} - 2\gamma w \frac{\partial T}{\partial y} \right) d\Omega \\
&+ \int_\Omega w(\boldsymbol{x}) d\Omega = 0
\end{aligned}$$

with $T(\boldsymbol{x}) = 0$ on S_a.

In this case, $S_a = \{(0,0)\}$.

4.3.3 Other approximations

Consider an SIS epidemic model in which individual infectious periods are distributed as any non-negative random variable Q of finite variance, and suppose that $R_0 = \beta E[Q] > 1$. Denote by p_Q the asymptotic (large N) probability, starting from a single infected individual in an otherwise susceptible population, that only a minor outbreak occurs. Denoting $g(\theta) = E\left[\mathrm{e}^{\theta Q}\right]$, the moment generating function of Q, then it is well-known (linear branching process approximation for minor outbreak) that p_Q is the unique solution in $[0,1)$ of

$$p_Q \quad = \quad g\left(-\beta\left(1-p_Q\right)\right).$$

Approximation of generalised infectious periods by Ball, Britton & Neal.

Another approximation of time to extinction from quasi-stationarity is derived from the work of Ball, Britton & Neal. In Lemma 3.2 of their 2016 paper, they find that in the case of $R_0 > 1$, $\tau \sim \tau^{\mathrm{BBN}}$, where τ is mean time to extinction from QSD, and

$$\tau^{\mathrm{BBN}} \quad = \quad E[Q]\sqrt{\frac{2\pi}{N}}\frac{1}{\left(R_0-1\right)\left(1-p_Q\right)}\exp\left(N\left(\left(1/R_0\right)-1+\ln R_0\right)\right). \tag{43}$$

In the case of the classic SIS model, then $p_Q = 1/R_0$ and Andersson-Djehiche formula is recovered.

When Q follows an Erlang distribution with mean $E[Q] = 1/\gamma$ and variance $1/k\gamma^2$, then moment generating function is $g(\theta) = (1 - (\theta/k\gamma))^{-k}$, so that p_Q is the unique solution in $[0, 1)$ of

$$p_Q \left(1 + R_0(1 - p_Q)/k\right)^k \quad = \quad 1. \tag{44}$$

For the case of $k = 2$, equation (44) is the cubic equation

$$\frac{1}{4}R_0^2 p_Q^3 - \frac{1}{2}R_0^2 p_Q^2 - R_0 p_Q^2 + \frac{1}{4}R_0^2 p_Q + R_0 p_Q + p_Q - 1 = 0.$$

which can be factorised to form

$$\frac{1}{4}(p_Q - 1)(R_0^2 p_Q^2 - R_0^2 p_Q - 4R_0 p_Q + 4) = 0, \tag{45}$$

resulting in solutions

$$p_Q \quad = \quad \frac{4 + R_0 \pm \sqrt{R_0\left(8 + R_0\right)}}{2R_0}, p_Q = 1.$$

Of these roots, only one is within $[0, 1)$. Therefore, we can substitute

$$p_Q \quad = \quad \frac{4 + R_0 - \sqrt{R_0\left(8 + R_0\right)}}{2R_0} \tag{46}$$

into (43). For the case of $k = 2$, the time to extinction can then be approximated by

$$\tau^{\mathrm{BBN}} \quad = \quad \frac{1}{\gamma}\sqrt{\frac{2\pi}{N}}\frac{2R_0}{(R_0 - 1)\left(R_0 - 4 + \sqrt{R_0\left(8 + R_0\right)}\right)} \exp\left(N\left((1/R_0) - 1 + \ln R_0\right)\right).$$

4.4 Comparison of approximations

4.4.1 Approximations of SIS - Erlang

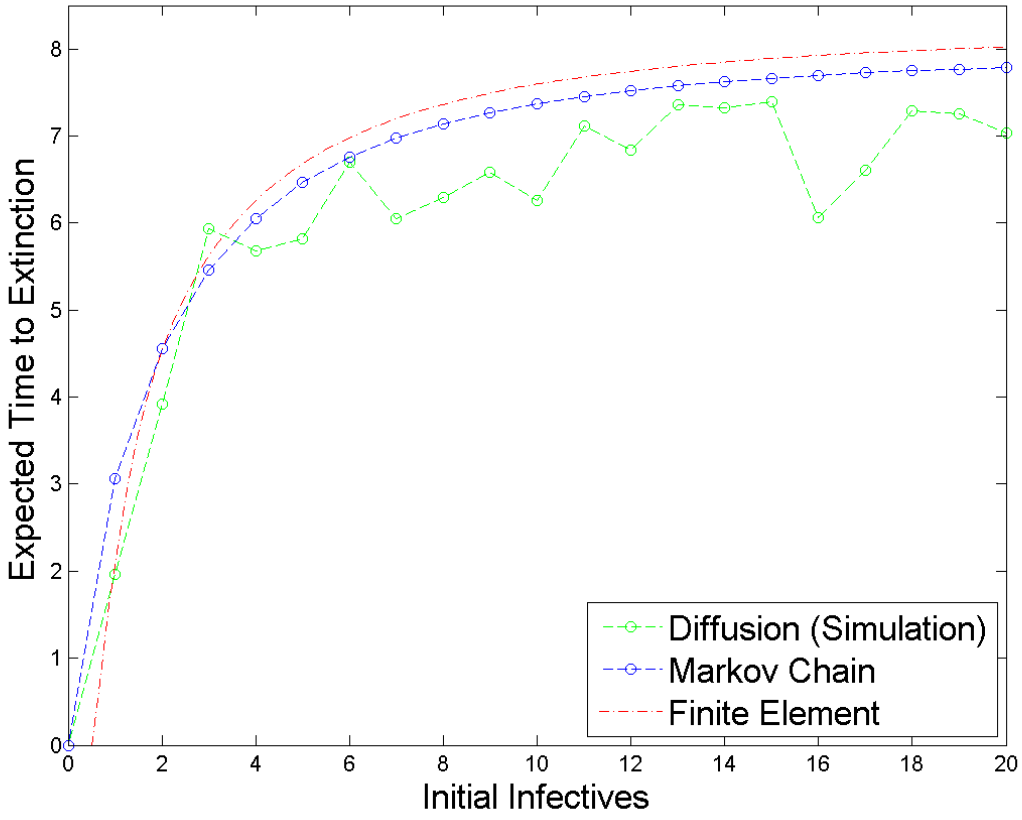

Figure 18: Comparison of the diffusion approximation to the exact values for SIS model with $k = 2$, with $N = 20$, $\beta = 1.2$, $\gamma = 1$. Simulation ran 100 times per data point.

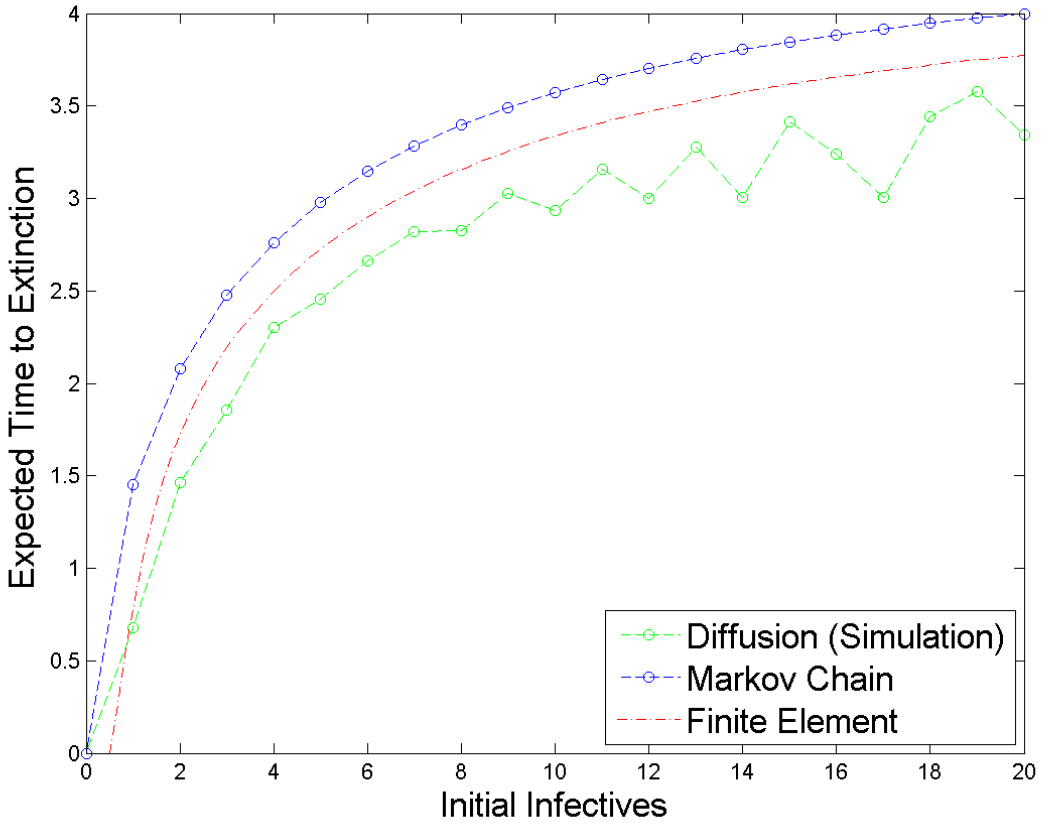

Figure 19: Comparison of the diffusion approximation to the exact values for SIS model with $k = 2$, with $N = 20$, $\beta = 0.6$, $\gamma = 1$. Simulation ran 100 times per data point.

In both figures (18) and (19), approximations are considered for the SIS Model with Erlang-distributed infectious period. In each case, the process is started from a number of infectives in the first infective stage, with none present in a second infective state, mimicking a naive infection.

Time to extinction appears well approximated in both cases, although the Finite Element method marginally overestimates time to extinction when $R_0 > 1$, but underestimates it in the case $R_0 < 1$.

As with the basic SIS model without demography, which can be considered a special case of this model where $k = 1$,the general shape of the figure remains the same, with the expected time to extinction plateauing as initial number of infectives increases towards N. Unlike in the basic SIS model without demography, the diffusion approximation underestimates the time to extinction for cases of $R_0 < 1$, although the picture is less clear in the case of $R_0 > 1$ due to the complexity of the diffusion simulation causing extremely long run times, leading to a non-smooth curve. For the case of $k = 2$, the diffusion approximation consistently underestimates the time to extinction, unlike its counterpart in

the case of $k = 1$. It does still remain a good fit to the original plot however, regardless of initial infectives.

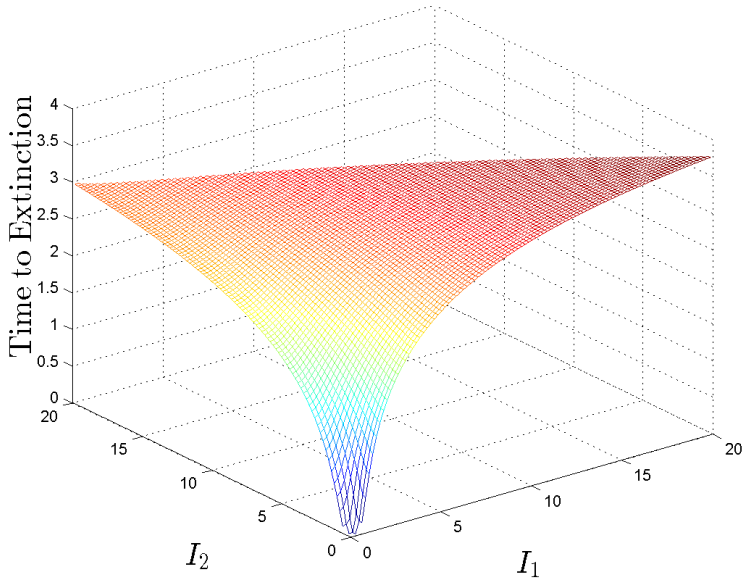

Figure 20: Plot of time to extinction calculated by finite element method for SIS model with $k = 2$, with $N = 20$, $\beta = 0.6$, $\gamma = 1$

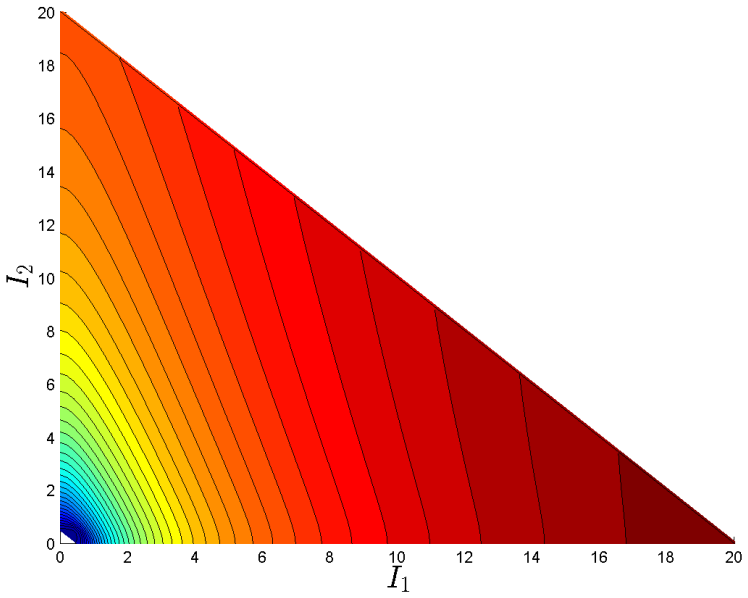

Figure 21: Contour plot of time to extinction calculated by finite element method for SIS model with $k = 2$, with $N = 20$, $\beta = 0.6$, $\gamma = 1$

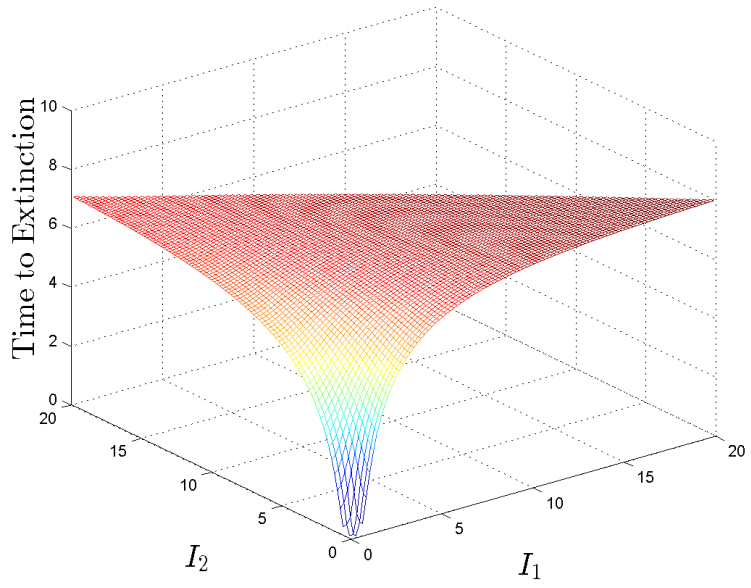

Figure 22: Plot of time to extinction calculated by finite element method for SIS model with $k = 2$, with $N = 20$, $\beta = 1.2$, $\gamma = 1$

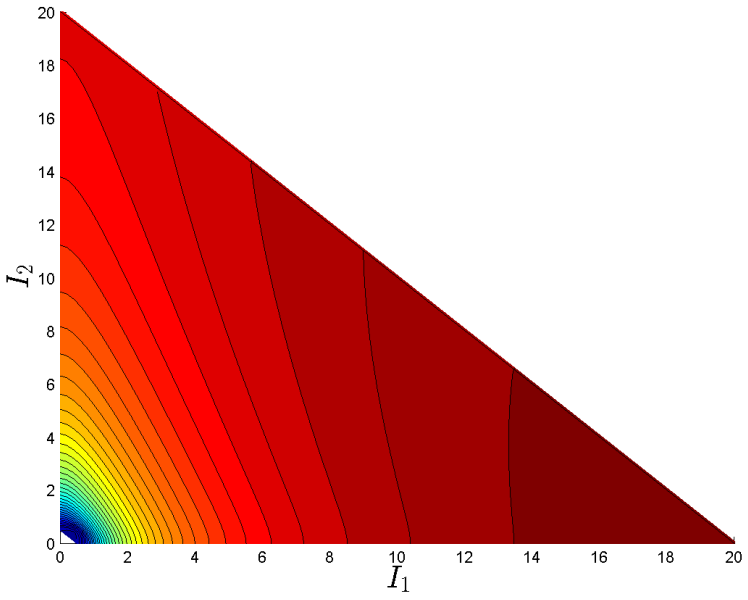

Figure 23: Contour plot of time to extinction calculated by finite element method for SIS model with $k = 2$, with $N = 20$, $\beta = 1.2$, $\gamma = 1$

The figures (20-23) also show the SIS Model with Erlang-distributed infectious period with process started from an initial number of infectives. In these figures however, the process is started from the

each possible combination of the individuals in infectious substates. In general, these diagrams allow for the consideration of time to extinction from any possible fixed initial state. As required by the finite element method, the continuity correction is made that the process becomes extinct when either$I_1 < 0.5$ or $I_2 < 0.5$). The provided contour plots do not readily demonstrate this due to the method of shading. This continuity correction is required as the time to hit any single state, such as $(0, 0)$ may not be finite.

The time to extinction for each of these cases again has diminishing returns relative to the initial number of infectives, however thetime to extinction from a variety of different states is not perfectly symmetrical between I_1 and I_2, as might have been suggested by (40).The differences in symmetry remains small for low values of I, but for values of $I \approx N$, such as the state $I = 20$ can produce times to extinction varying by greater than 10% depending on the initial infectious substage.

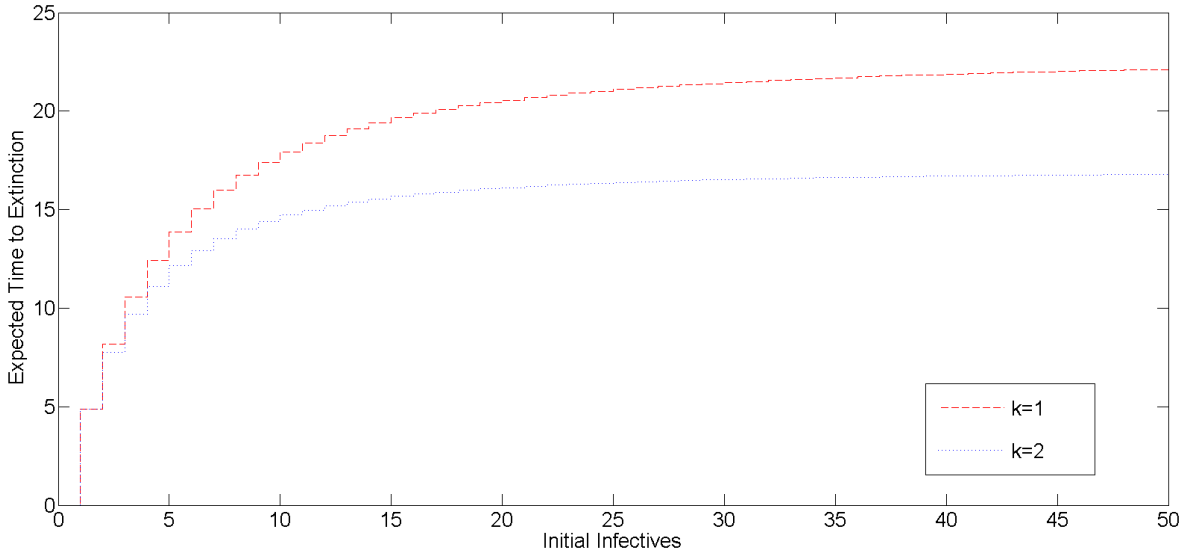

Figure 24: Diagram comparing the expected extinction times for SIS models with $k = 1, 2$ infectious stages, with $N = 50$, $\beta = 1.2$, $\gamma = 1$. Expected extinction times calculated exactly via Markov chain method.

Figure (24) compares the SIS Model with Erlang-distributed infectious periods with that of the basic SIS Model, as it is a special case of the former, taking $k = 1$. It can be seen in this figure that the overall shape of the graph remains the same, although the case of 2 infectious substages produces a model with a decreased persistence time, all other parameters being kept the same; this result is in line with the deterministic approximation of Lloyd (2000). The difference in persistence between the cases $k = 1$ and $k = 2$ is small at low values of initial infectives, and increases once the number of initial infectives exceeds

the deterministic equilibrium value for these parameter values.

In figure (24) the initial infectives for the model of $k = 2$ are started in the first infectious substage.

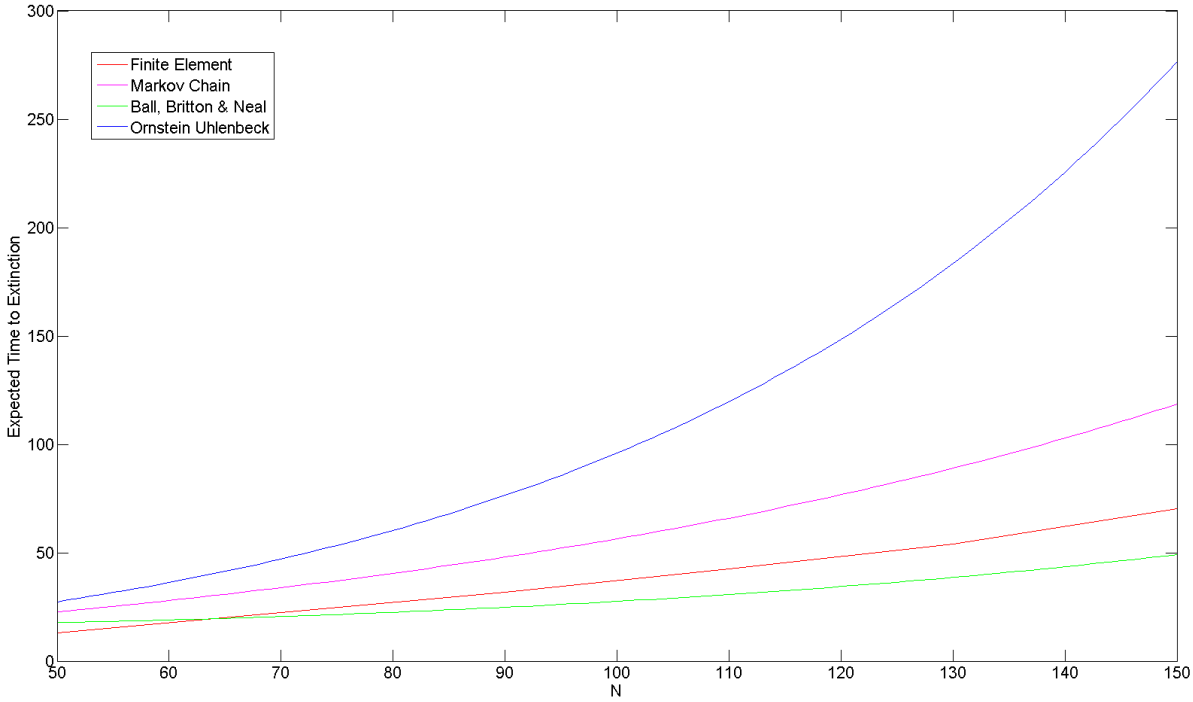

Figure 25: Diagram comparing the approximations of expected extinction times for SIS model with $k = 2$ infectious stages, with $N \in (50, 150)$, $\beta = 1.2$,$\gamma = 1$.

Figure (25) compares the time to extinction from quasi-stationarity for a variety of previously considered approximations.

As with the previous figures considering initial infectives, the Finite Element method again underestimates time to extinction relative to the calculated Markov chain values. The Ornstein-Uhlenbeck approximation is weak here, consistently overestimating time to extinction, although this is to some extent expected as the Ornstein-Uhlenbeck approximation does not in general perform well for approximations of larger R_0 values, and again diverges as N increases. The approximation of Ball, Britton and Neal (2016) also underestimates the expected time to extinction. Their approximation is apparently less accurate than that of the Finite Element method, although it can be seen to be much quicker and easier to compute.

As with the case of $k = 1$, i.e. the basic SIS Model, the Ornstein Uhlenbeck approximation quickly

diverges as with Figure (6) which also has parameter values of $R_0 = 1.2, \gamma = 1$. Whilst in the case of $k = 1$, no approximations underestimated time to extinction, in the case of $k = 2$ shown in figure (25) the Ornstein-Uhlenbeck is the only approximation not to underestimate persistence time.

Figures (20-23) considers the full range of possible initial states, but as this model is not memoryless, strong arguments can be made for considering the model started from the initialisation stage where all infectives begin in the first infectious substage(figure 24), or from quasi-stationarity, which the system is likely to have reached (figure 25). The results between these different starts do not vary greatly, however several approximations are based around the assumption of quasi-stationarity due to their origins in previous work and therefore cannot easily be assessed for fixed values.

5 Analysis of Andersson and Britton (2000)

The work of Andersson and Britton considered a model with Erlang-distributed periods and drew several conclusions. In the process of comparing results with their work, I found several potential discrepancies which when assessed more closely were indeed found to have been inaccurate.

5.1 Model Formulation

Andersson and Britton (2000) studied an SEIR model as described earlier in figure 3.This model is an SEIR model with Erlang distributed rates for Susceptible, Exposed and Infected periods, as well as demography. Taking $i = j = k = 1$, transition rates for their model are as follows.

Event	State transition	Transition rate
Birth of susceptible	$(S, E, I) \to (S + 1, E, I)$	μN
Death of susceptible	$(S, E, I) \to (S - 1, E, I)$	μS
Infection of a susceptible	$(S, E, I) \to (S - 1, E + 1, I)$	$\frac{\beta}{N} SI$
Progression of infection	$(S, E, I) \to (S, E - 1, I + 1)$	λE
Death of infected	$(S, E, I) \to (S, E, I - 1)$	$(\mu + \gamma)I$

Here $\mu, \gamma, \lambda, \beta > 0$, are the rates of demography, additional infective death, rate of leaving the latent phase and infection respectively. For this model, the basic reproduction number is $R_0 = \frac{\beta}{\gamma}$.

Also studied were models taking $\{i = j = k = 2\}$, $\{i = j = k = 3\}$, $\{i = j = 1, k = 2\}$ and $\{i = j = 1, k = 3\}$.

Andersson and Britton (2000)'s analysis of the above model showed some behaviour which appeared to change when analysed at $N = 10^5$ and $N = 10^6$, as shown in table 1. Specifically, the dependence of time to extinction for R_0, denoted by them as R and the Coefficient of Variation of life length. This switching behaviour is unexpected for these parameter values, as the model is not expected to reach the state of total or near-total infection, and as such the expected relationship between R_0 and time to

extinction is monotonically increasing and may be considered an artefact of approximation.

In order to calculate their results, Andersson and Britton (2000) used an Ornstein-Uhlenbeck approximation, followed by a further approximation derived taking the parameter ϵ small, allowing for the removal of terms of order $O(\epsilon^2)$ or greater. I discovered discrepancies between the Covariance matrix of the approximation and an equivalent matrix created by simulation, when $N = 10^5$. Further simulation work has determined these differences are not due to the second approximation stage but within the Ornstein-Uhlenbeck approximation itself, as simulated graphs of S, E, I at the parameter values used at $N = 10^5$ show non-normal behaviour. These differences can be demonstrated by comparing their approximation expected time to extinction with simulated results.

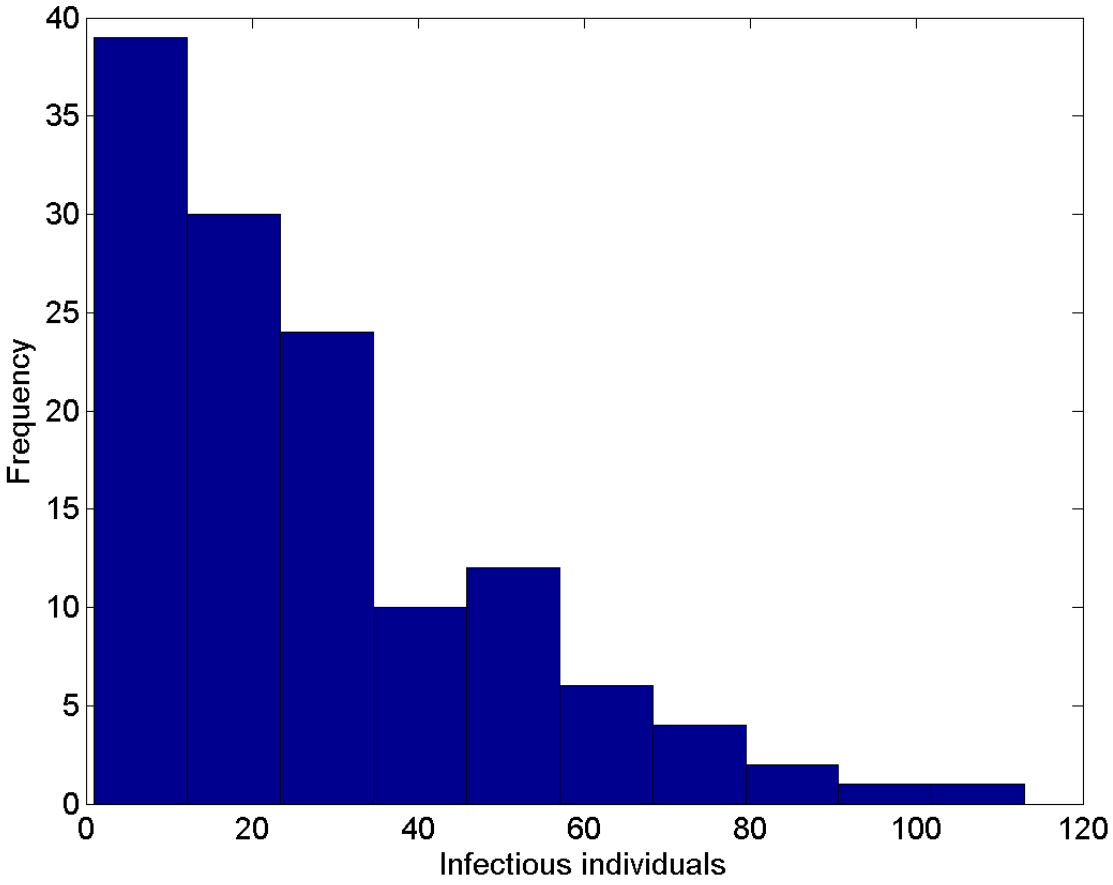

Figure 26: The long term behaviour of the Infective population in Andersson and Britton's model for their parameter values of $N = 10^5, r = 1, \mu = \frac{1}{70}, R_0 = 15, \gamma = 52, \beta = 780, i = 1, j = 1, k = 1$. This figure was created by considering the simulated distribution of Infectives the SEIR model, started from deterministic equilibrium, at a time deemed to be sufficient to allow the model to reach quasi-stationarity.

Figure 26 demonstates the problems with approximating the model with an Ornstein-Uhlenbeck approximation at these parameter values. Note how the graph does not appear approximately normally distributed, but is instead heavily skewed. This skew results in the deviations in the approximation which have been demonstrated.

However, Andersson and Britton's approximations remain valid when $N = 10^6$, as the quasi-stationary distribution displays more normal behaviour.

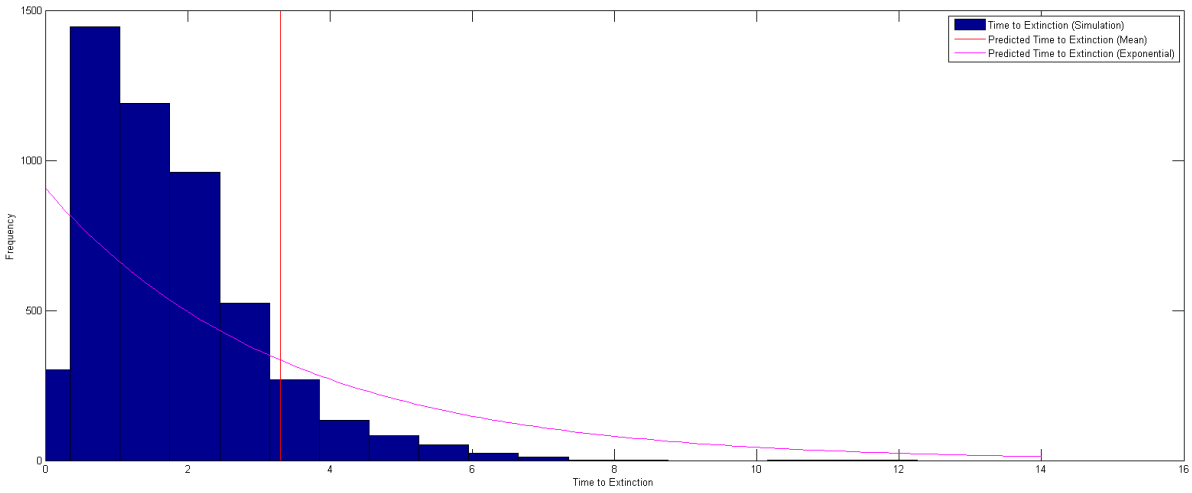

Figure 27: Histogram of simulated time to extinction from deterministic equilibrium for SEIR model of Andersson and Britton (2000), as stated in figure 3 and parameter values: $N = 10000, \mu = \frac{1}{70}, \beta = 780, \gamma = 52, i = 1, j = 1, k = 1$. Also shown is the mean of the simulations, and the value predicted by Andersson and Britton's approximation, as well as an exponential distribution based on their approximation. The simulations were started from deterministic equlibrium, but were allowed to 'burn in' for a period of time, allowing the simulations to approach the quasi-stationary distribution, and removing any simuations that had already gone extinct.

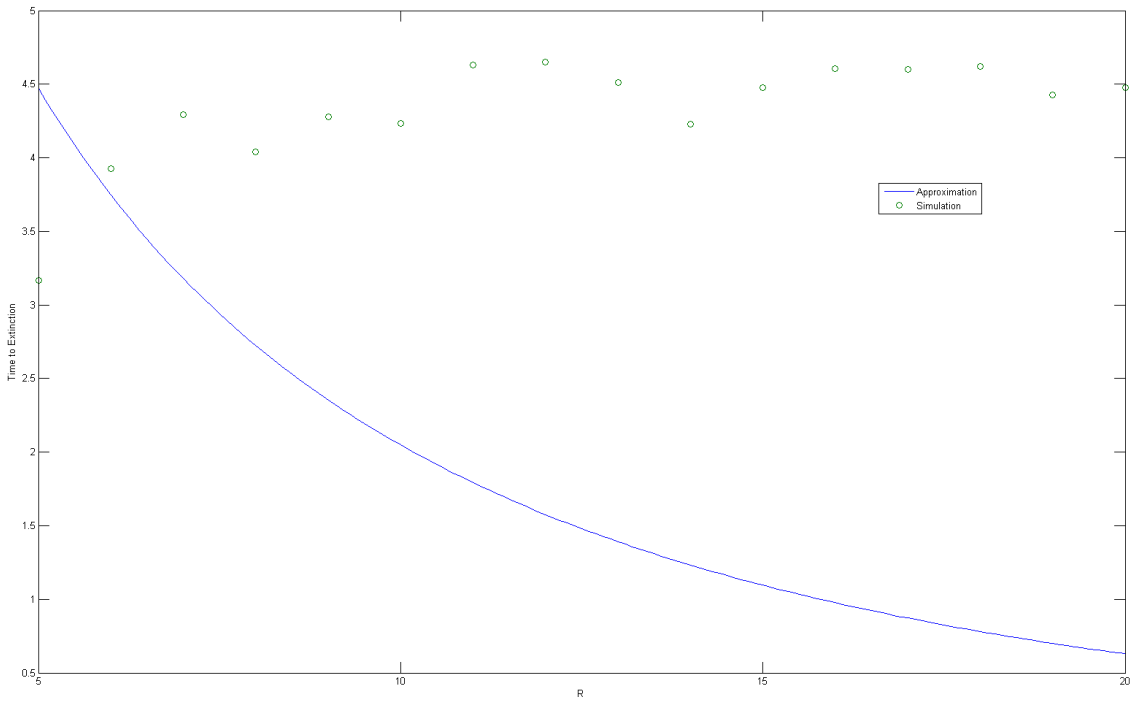

Figure 28: Andersson and Britton's approximation formula, compared to simulated time to extinction, started from deterministic equilibrium, as R_0 varies. $N = 10^5, r = 1, \mu = \frac{1}{70}, \gamma = 52, \beta = 780$. Each point is the average of 1000 simulations.

Andersson and Britton claim that time to extinction decreases as R_0 decreases with $N = 10^5$, but increases if $N = 10^6$. Figure 28 does not show a decreasing trend, and appears to be steady over the range considered, or indeed marginally increasing in a case of $N = 10^5$.

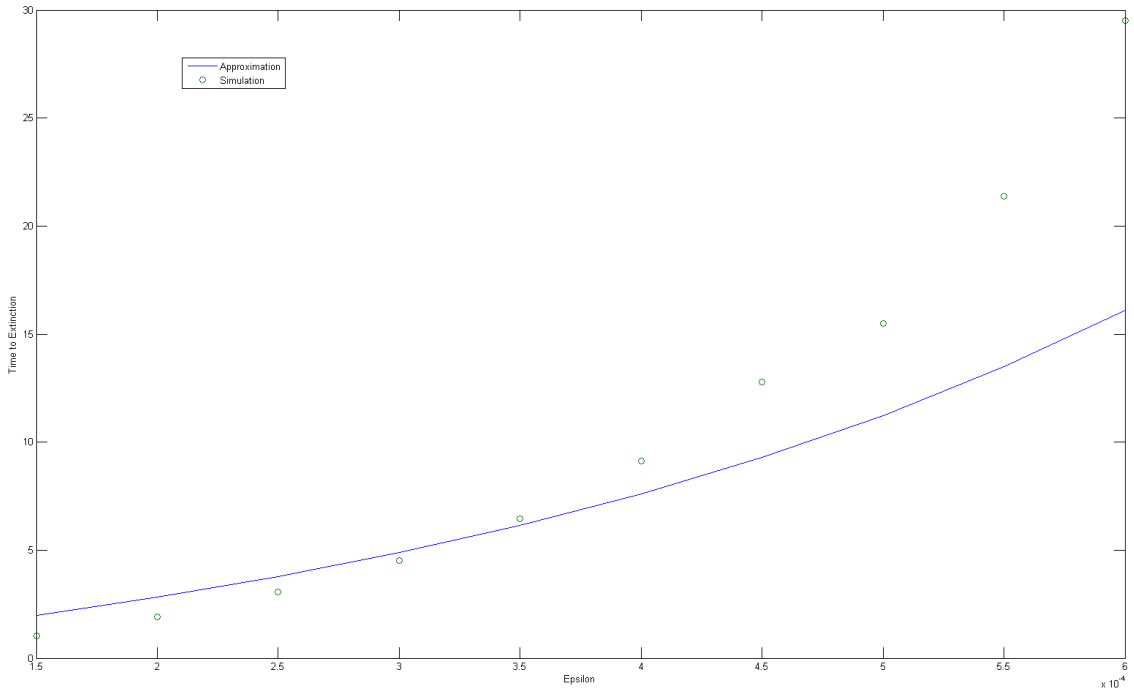

Figure 29: Andersson and Britton's approximation formula, compared to simulated time to extinction, started from deterministic equilibrium, as ϵ varies. $N = 10^5, r = 1, \mu = \frac{1}{70}, R_0 = 15, \gamma = 52, \beta = 780$. Each point is the average of 1000 simulations.

Figure 29 is seen to be in good agreement with the approximation of Andersson and Britton. For this variable ϵ, it predicts a positive relationship with time to extinction at both $N = 10^5$ and $N = 10^6$.

Andersson and Britton (2000) also proposed proportionality between Critical Community Size and $\frac{1}{\epsilon^2}$; simulated evidence for this is time consuming to produce computationally, and as such was limited in the paper. The Critical Community Size (CCS) is defined as the population size above which fadeout of a disease over a given period is less probable than not. Andersson and Britton's Critical Community Size was defined as the value of N for which $47 - 53\%$ of simulations had become extinct by time $\frac{1}{\mu}$. This was defined due to limitations in precision for their approximation.

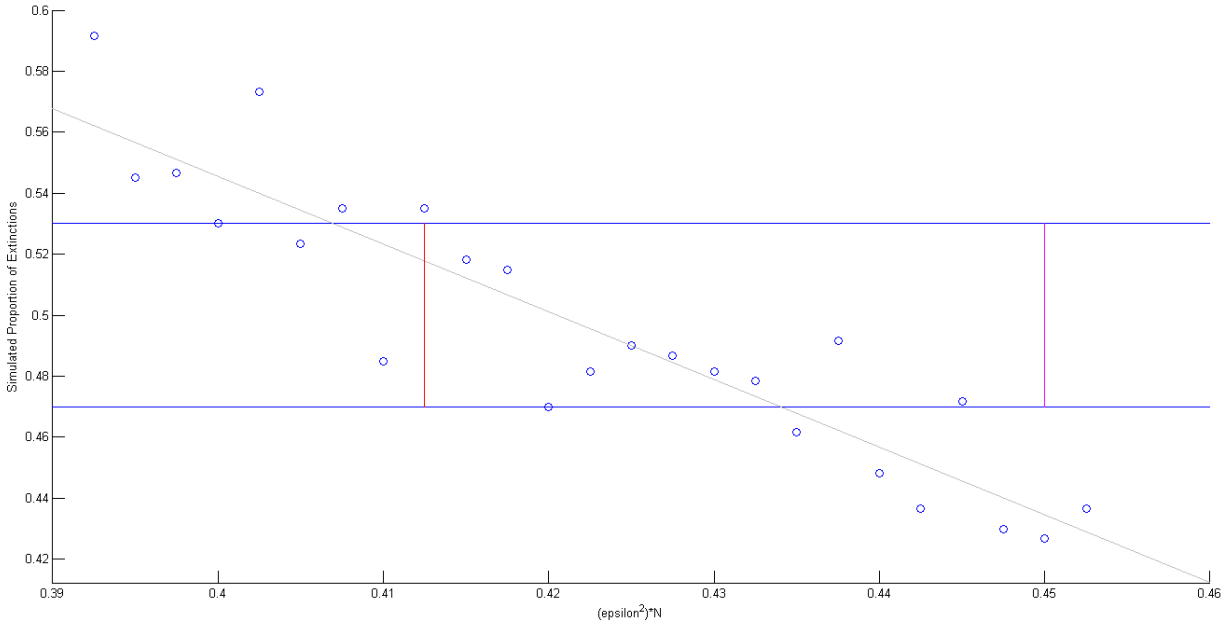

Figure 30: Simulated proportion of extinctions by time $\frac{1}{\mu}$ for given N values $i = 1, j = 0, k = 3, \beta = 240, \gamma = 20, r = 1, \mu = \frac{1}{70}, N \in [50000, 55000]$

Figure 30 attempts to find the critical community size, defined by Andersson and Britton (2000). In the graph, this is represented by the area between the two horizontal blue lines. Their proposed value for the critical community size, where the proportion of extinctions should transition into $47 - 53\%$ is pictured in red, and their simulated result for critical community size is pictured in pink. My simulated results in the area show good agreement with their results, as the transition into the $47 - 53\%$ region occurs at similar parameter values.

Andersson and Britton (2000) calculate an approximation for ρ, the proportion of states with exactly one infective remaining $q_{\bullet,1}$ that are in the final substage of infection $q_{\bullet,0,e_k}$. That is, $\rho = \frac{q_{\bullet,0,e_k}}{q_{\bullet,1}}$ This value ρ is key in the calculation of time to extinction as it partially defines the hazard rate, the odds of being in the state $I = 1$, and therefore the expected time to extinction. A process can only become extinct when in the final substage of infection, so the ρ values acts to modify the standard hazard rate of a non-Erlang distributed infectious period.

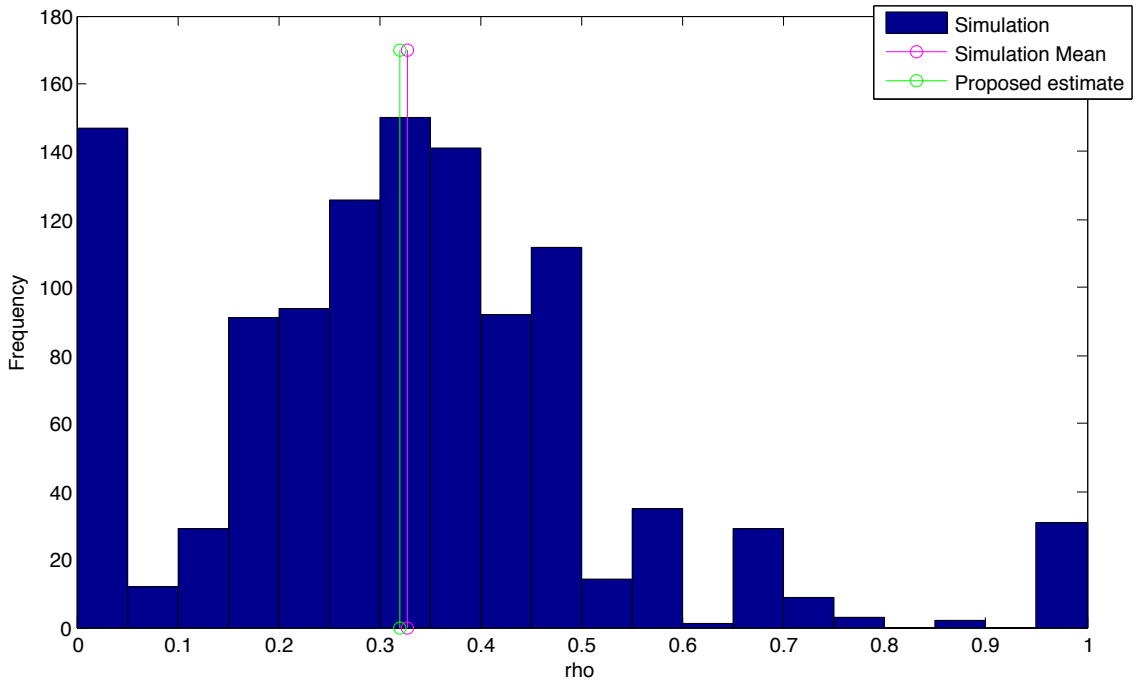

Figure 31: Simulated values of ρ, shown against Andersson and Britton's proposed approximation of ρ Parameter values $N = 10^5, r = 1, \mu = \frac{1}{70}, R_0 = 15, \gamma = 52, \beta = 780$.

Intuitively, an estimation for ρ in a model with k substages of infection is $\frac{1}{k}$, as all stages remain occupied for an equal amount of time, allowing for an equal probability to be in each stage. Using this value in the approximation for Time to extinction formulae of Andersson and Britton (2000) results in an alternative approximation.

N	Time to Extinction (Simulation)	Time to Extinction (Approximation)	Time to Extinction ($\rho = \frac{1}{3}$)
10^5	2.5605	2.6254	2.5172
10^6	33.3627	34.2857	35.7589

Table 3. Comparison of Times to Extinction, with parameter values $r = 1, \mu = \frac{1}{70}, R_0 = 15, \gamma = 52, \beta = 780$, the parameter values of Andersson and Britton (2000). Both Time to Extinction (Approximation) and Time to Extinction ($\rho = \frac{1}{3}$) rely on a further approximation by Andersson and Britton given

the value of ρ.

Notably, for $N = 10^5$ the alternative simpler approximation of $\frac{1}{k}$ performs slightly better, but this is not the case for $N = 10^6$, although the simpler approximation does not perform much worse.

The initial motivation for this work was the consideration of the trend of persistence time with respect to R_0 in the case of $N = 10^5$, as it did not fall in like with the expected result based on other Erlang-distributed work. As a result of empirical work it was shown that the original theoretical work in this particular case had given an inaccurate result, however this was mainly proven using computational power unavailable to Andersson and Britton at the time of publishing. As a result of a further assessment as to where the fault in the methodology was, it was largely found that the main flaw could be found in the lack of normality in the quasi-stationary distribution, a necessity for the usage of an Ornstein-Uhlenbeck approximation. That the approximation of Andersson and Britton (2000) was found to be inaccurate in the case of a non-normal distribution was mirroed by similar experiences in my own attempts to find an approximation derived from the Coefficient of Variation, as seen in Figure (16). Additionally, the creation of an alternative, simpler, methodology for approximating ρ was found.

6 Conclusions

We have primarily formulated and analysed the behaviour of 4 different families of deterministic and stochastic models: SIS, SIR with demography, SIS with Erlang distributed infectious periods, SEIR with demography and Erlang distributed infectious periods. We have focussed on the suitability of approximations, particularly with respect to approximations of disease persistence, the accuracy of these approximations, and the necessary computational power for these approximations..

Lloyd (2000) found that for SIR models, Erlang-distributed infectious periods diminish disease persistence. My results here for SIS models agree with this assessment. Models with more realistic distributions die out more quickly, even as the mean time spent in the infectious period remains the same. That is, persistence may be overestimated in many simplified models. Lloyd (2000) notes that "The use of realistic IPDs [infectious period distributions] increases variability and hence the frequency of episodes in which the number of infectives falls to low levels'.' When the sum of infectives are considered, the variability is as calculated in agreement with Lloyd (comparative to the model - Lloyd studied the SIR model), Note that Lloyd only used simulation, and stability of deterministic system to come to conclusions. The addition of Erlang-distributed infectious periods to the model therefore demonstrate predictability in their application, and may be a complication simple enough to therefore be worthy of further study. Generalised non-gamma distrbuted infectious periods remain an area of great interest, and this particular model shows itself to be amenable to analysis.

Andersson and Britton (2000) note for the SEIR model that "When the process is close to the absorbing barrier i.e. when there are few infectives, it moves at a slower rate than the approximating diffusion", an effect noticed in my own results here for the SIS model. There is a shorter time to extinction for the diffusion approximation than the exact result calculated via Markov chain in the case of $k = 2$. This is in contrast to the case of $k = 1$, where the exact result becomes extinct quicker than the diffusion system.

Attempts to find an improved approximation fell into similar results as that of Andersson and Britton (2000), with the approximation created only remaining valid during the time when the quasi-stationary distribution resembles a normal distribution. Attempts were made to find parameter values for which such normality is expected, and whilst this range seems large and contains several potentially realistic parameter values, it demonstrates the overall lack of requirement for a quasi-stationary distribution to

resemble a normal distribution after any normal amount of burn in. As such, the models considered cannot be found to always have a best approximation, a conclusion supported by the variety of graphs drawn showing assorted parameter values and models.

Empirical work demonstrating the approximations and simulating the processes involved in several models showed the strengths of various models. Some models rely on large population sizes to be valid, such as the deterministic and the approximation of Andersson and Djehiche (1998), and this is not always a sensible assumption, although the results for the parameter values taken in this work find it to be adequate. The Ornstein-Uhlenbeck approximation in particular is found to have particular weakness in approximation, but this is to be expected due to the ease of calculation, and as such remains a valid option in many cases.

6.1 Directions for further work

SIR model with demography, with Erlang distributed infectious periods

Event	State transition	Transition rate
Birth of susceptible	$S \to S + 1$	μN
Death of susceptible	$S \to S - 1$	μS
Infection of susceptible	$I_1 \to I_1 + 1$	$\frac{\beta}{N}\left(N - \sum_{m=1}^{k} I_m\right)\left(\sum_{m=1}^{k} I_m\right)$
Transition to next infectious substage	$I_m, I_{m+1} \to I_m - 1, I_{m+1} + 1$	$k\gamma I_m \ (m = 1, ..., k-1)$
Death of infected	$I_m \to I_m - 1$	$\mu I_m (m = 1, ..., k-1)$
Removal of infected	$I_k \to I_k - 1$	$(k\gamma + \mu) I_k$

Many of the methods previously used can be adapted for use with the SIR model with demography, with Erlang distributed infectious periods. With more time, further analysis of this model for comparison would have been investigated, in particular the analysis of the variety of approximations able to be adapted to fit the variety of approximations shown to be valid for the SIS model with Erlang-distrbuted infectious periods.

Whilst some work was completed on this topic, its similarity to the model of Andersson and Britton (2000) ultimately led to the majority of the work being repurposed.

7 Appendices/Code

7.1 Freefem++

This code for calculating time to extinction from varying initial states using Freefem++. In this example, $\beta = 0.6, \gamma = 1, \epsilon = 0.5, N = 20$.

```
// set parameter values
real gamma=1., beta=0.6, epsilon=0.5, n=20.;
// defining the boundary
border B2(t=epsilon,n){x=t; y=0;}
border B3(t=0,n){x=n-t; y=t;}
border B4(t=0,n-epsilon){x=0; y=n-t;}
border B1A(t=0,epsilon){x=t; y=epsilon;}
border B1B(t=0,epsilon){x=epsilon; y=epsilon-t;}
// define mesh
mesh Th = buildmesh (B2(100)+B3(100)+B4(100)+B1B(5)+B1A(5));
plot(Th,wait=true);
// define finite element space, piecewise quadratic
fespace Vh(Th,P2);
Vh tau,w;
// solve PDE
solve Backward(tau,w,solver=LU) =
int2d(Th)(-((beta/(2*n))*(x+y)*(n-x-y)+gamma*x)*dx(tau)*dx(w)
-gamma*(x+y)*dy(tau)*dy(w)
+gamma*x*dy(tau)*dx(w)
+gamma*x*dx(tau)*dy(w))
+int2d(Th)(2*gamma*(x-y)*w*dy(tau)
+((beta/n)*(x+y)*(n-x-y)-2*gamma*x-(beta/(2*n))*(n-2*x-2*y)-gamma)*w*dx(tau))
-int2d(Th)(-w)
+int1d(Th,B2)(gamma*x*w*dx(tau))
+int1d(Th,B3)((1/sqrt(2.0))*gamma*y*w*dy(tau))
+ on(B1A,tau=0)
+ on(B1B,tau=0) ; // Dirichlet boundary condition
plot(tau,value=true,fill=true,wait=true);
// save B06.points and B06.faces file
savemesh(Th,"B06",[x,y,tau]);
```

Files generated using this code can be imported into MATLAB.

7.2 MATLAB

7.2.1 Approximations time to extinction from a range of initial states for the SIS Model

Code as used in figure (5).

```
%Time to extinction from various initial states.
%Diffusion Approximation, Deterministic and Markov Chain.

% model parameters
N = 50;
beta = 0.3;
g = 1;
%Diffusion
%Diffusion parameters
a = 0;
b = N;
mu = 0;
lambda = 0;
%Discretization parameters
M = 900000;
h = (b-a)/M;
%Soln
x=a:h:b;
A_of_x = (beta/N)*(N-x).*x - g*x;
B_of_x = (beta/(2*N))*(N-x).*x + (g/2)*x;

phi = h * A_of_x + B_of_x;
phi_tilda = [0,phi(2:length(phi)-1)];
xi = -h * A_of_x - 2*B_of_x;
xi_tilda = [-h^2, xi(2:length(xi)-1),-1];
psi_1 = B_of_x(2:length(B_of_x)-1);
psi_tilda = [psi_1,1];

S = gallery('tridiag',psi_tilda,xi_tilda,phi_tilda);
rhs = [-mu*h^2,-ones(1,M-1)*h^2,h*lambda]';
```

```
T = S \ rhs;


%Deterministic
gamma=g;
for init=0:N
Deterministic(init+1)=-log((init.*(2.*beta.*N-2.*gamma.*N-beta))./(-beta.*init+beta.*N-
    gamma.*N))./(beta-gamma);
end
%This Formula derived using Maple (See DetermFullSoln.mw)
Deterministic(1)=0;
 %This Approximation is only valid for R_0 < 1


%Eigenvalue/Exact
R_0=beta./gamma;
Trans=zeros(N+1); %Preallocate Matrix
%Populate Matrix
for i=2:N
Trans(i,i-1)=gamma.*(i-1);
Trans(i,i)=-( gamma.*(i-1) + beta.*(i-1).*(N-i+1)./N ) ;
Trans(i,i+1)=beta.*(i-1).*(N-i+1)./N;
end
Trans(N+1,N)=gamma.*N;
Trans(N+1,N+1)=-gamma.*N;


TransTruncated=Trans(2:end,2:end); %Throw away case of I=0
[E,V]=eigs(TransTruncated',1,'LR'); %Select Correct Eigenvalue/vector
Quasi=E./sum(E); %Normalise
alpha=-transpose(ones(1,N));


TTESTATE=TransTruncated\alpha;
Extinct_TheoryF=1./(gamma.*Quasi(1)); %Mean Time to Extinction (Theory)
Extinct_TheoryF;


minusone1=-ones(max(size(TransTruncated)),1);
TauEach1=TransTruncated\minusone1;
```

```
%Kryscio and Lefevre/Andersson and Djehiche
R=beta/g;
gamma=g;
eulergamma=-psi(double(1));
KL_approx = (vpa(eulergamma) + log(1:N) + log(1-R.*(1-(1/N:1/N:1)))).(gamma-beta.*(1-(1/
    N:1/N:1)));

%Linear birth-death process
Linear_BD = (  (1-(1./R).^(1:N)).*log(1-R) + cumsum(1./(1:N)) - cumsum(R.^(1:N)./(1:N))./
    R.^(1:N) )./(gamma-beta);

%Figure section
FIG=figure;
plot(x,T,'g'); hold on
plot([0:N],Deterministic);
plot(0:N,[0;TauEach1],'r','LineStyle','none','marker','o');
plot(1:N,double(KL_approx),'y');
plot(1:30,Linear_BD(1:30),'m')
xlabel('Initial Infectives','FontSize',16);
ylabel('Expected Time to Extinction','FontSize',16);
leg=legend('Diffusion','Deterministic','Markov Chain','Andersson and Djehiche','Linear
    Birth-Death','Location','southeast')
set(leg,'FontSize',16);
print('SIS_ISTATE_03','-dpng');
print('SIS_ISTATE_03','-deps');
saveas(FIG,'SIS_ISTATE_03','fig')
```

7.2.2 Approximations of expected time to extinction from quasi-stationarity for the SIS model

Code as used in Figure (6).

```
Nstart=100;
Nend=1000;

beta=1.2;
gamma=1;
```

```
R_0=beta./gamma;

%Markov (exact)

%Preallocate Matrix
Trans=sparse(zeros(N+1).^2);
for N=Nstart:10:Nend

%Populate Matrix
for i=1:((N+1).^2)-(N+1)
    i1=floor((i-1)./(N+1));
    i2=rem(i-1,N+1);
    Trans(i,i+N+1)=(i1+i2<=N).*(beta./N)*(N-i1-i2).*(i1+i2); %A
end

for i=(N+1):(N+1).^2
     i1=floor((i-1)./(N+1));
    i2=rem(i-1,N+1);
    Trans(i,i-N)=(i1+i2<=N+1).*(i2~=N).*(2.*gamma.*i1); %B
end

for i=2:(N+1).^2
       i1=floor((i-1)./(N+1));
    i2=rem(i-1,N+1);
    Trans(i,i-1)=(i1+i2<=N+1).*(i2~=0).*(2.*gamma*i2); %C
end


for i=1:(N+1).^2
Trans(i,i)=-sum(Trans(i,:));
end

Temp=Trans;

for i=1:(N+1).^2

     i1=floor((i-1)./(N+1));
```

```
    i2=rem(i-1,N+1);

    if i1+i2>=N+1
Temp(i,:)=(NaN);
Temp(:,i)=(NaN);
    end
end
Temp(all(isnan(Temp),2),:)=[];
Temp(:,all(isnan(Temp),1))=[];

TempTruncated=Temp(2:end,2:end);
[E1,V1]=eigs(TempTruncated',1,'LR');
Quasi1=E1./sum(E1); %Normalise

Extinct_Theory1(1+N-Nstart)=1./(gamma.*Quasi1(1)); %Mean Time to Extinction (Theory)
end

figure
plot(Nstart:Nend,Extinct_Theory1)
```

7.2.3 Coefficient of variation based approximation, with test for normality included

Code as used in figure (16), based on equation (38).

```
clear all
%points=input('Number of Simulations: ');
points=15;
%sim per point
numsim=40;
%N
Nmin=250;
Nmax=350;
%R0
Rmin=8;
Rmax=12;
%Alpha
Amin=35;
```

```
Amax=45;
%Gamma
Gmin=0.15;
Gmax=0.15;

NRAG=[Nmin+randi(Nmax-Nmin,1,points);Rmin+((Rmax-Rmin).*rand(1,points));Amin+((Amax-Amin)
    .*rand(1,points));Gmin+((Gmax-Gmin).*rand(1,points))];

Tmata=zeros(numsim,points);

parfor sim=1:points
    N=NRAG(1,sim);
    R0=NRAG(2,sim);
    alpha=NRAG(3,sim);
    gamma=NRAG(4,sim);

    beta=R0.*alpha.*gamma;
    mu=.2/(alpha-1);
    Tmax=10000;
    QStime=1./mu;

    Tend=zeros(numsim,1); %preallocating
    Send=zeros(numsim,1); %preallocating
    Iend=zeros(numsim,1); %preallocating
    Tmat=zeros(numsim,1); %preallocating
    SAMP=zeros(numsim,1);

    for i=1:numsim
        TRIG=0;
        %Population Param
        S=round((mu+gamma)*N/beta);
        I=max(1,round((mu*N)*(1-((mu+gamma)/beta))/(mu+gamma)));
        Istar=I;
        t=0; %time step
        T=0; %Total time
```

```
while I>0 && T < Tmax %Stops when no infected
    a=mu*S;
    b=mu*N;
    c=(gamma+mu)*I;
    d=(beta/N)*S*I;
    rate=a+b+c+d;

    time=random('Exponential',1/rate); %decide when next step

    U=rand*rate;
    if U<a
        S=S-1;
    elseif U<a+b
        S=S+1;
    elseif U<a+b+c
        I=I-1;
    else
        I=I+1;
        S=S-1;
    end %decide which next step

    if T>=QStime && TRIG==0
        SAMP(i)=I;
        TRIG=1;
    end

    t=t+1;
    T=T+time;
    Send(i)=S;
    Iend(i)=I;
    Tmat(i)=T;

end
if I==0 && t>1
    Tend(i)=Tmat(i);
elseif I==0 && t==1
    Tend(i)=0;
```

```
            else
                Tend(i)=Tmax;
            end


    end
Tmata(:,sim)=Tend;
TTE(sim)=mean(Tmata(:,sim));
QS(sim)=mean(SAMP);
QSDist(:,sim)=SAMP;
JB(sim)=jbtest(SAMP);
VarianceI=(R0-1+((mu./(mu+gamma)).*R0.^2));
MeanI=mu.*(R0-1)./(R0.*(gamma+mu));



CV=sqrt(N*VarianceI)./(N.*MeanI);
CV1(sim)=CV;
Form(sim)=(CV*MeanI*N*sqrt(2*pi)./gamma).*(exp(1./(2.*(CV.^2))));
end
Form1=Form;
Correct=sqrt(2.*pi).*(NRAG(2,:)-1)./(NRAG(4,:).*NRAG(3,:).*NRAG(2,:));

Form1=Form1.*Correct;

SIMRES=TTE;
JB=transpose(JB);

SUCC=SIMRES.*transpose(1-JB);
FAIL=SIMRES.*transpose(JB);

SUCC(SUCC==0)=NaN;
FAIL(FAIL==0)=NaN;

figure
scatter(SUCC,Form1,'g')
hold on
scatter(FAIL,Form1,'r')
```

```
Normals=1-JB;
```

7.2.4 Approximations time to extinction from a range of initial states for the SIS Model with Erlang distributed infectious periods

Code as used in figure (18).

```
%Draws k2_N20_B12


clear all


load('Tmat2_k2_N20_B12.mat')
N=20;
beta=1.2;
gamma=1;

a_Fig=figure;
plot([0:N],Tmat2,'--og','markers',5);



%Preallocate Matrix
Trans=sparse(zeros(N+1).^2);



%Populate Matrix


for i=1:((N+1).^2)-(N+1)
    i1=floor((i-1)./(N+1));
    i2=rem(i-1,N+1);
    Trans(i,i+N+1)=(i1+i2<=N).*(beta./N)*(N-i1-i2).*(i1+i2); %A
end


for i=(N+1):(N+1).^2
     i1=floor((i-1)./(N+1));
    i2=rem(i-1,N+1);
```

```
    Trans(i,i-N)=(i1+i2<=N+1).*(i2~=N).*(2.*gamma.*i1); %B
end

for i=2:(N+1).^2
       i1=floor((i-1)./(N+1));
    i2=rem(i-1,N+1);
    Trans(i,i-1)=(i1+i2<=N+1).*(i2~=0).*(2.*gamma*i2); %C
end



for i=1:(N+1).^2
Trans(i,i)=-sum(Trans(i,:));
end

Temp=Trans;

for i=1:(N+1).^2

     i1=floor((i-1)./(N+1));
    i2=rem(i-1,N+1);

    if i1+i2>=N+1
Temp(i,:)=(NaN);
Temp(:,i)=(NaN);
    end
end

Temp(all(isnan(Temp),2),:)=[];
Temp(:,all(isnan(Temp),1))=[];

TempTruncated=Temp(2:end,2:end);
[E1,V1]=eigs(TempTruncated',1,'LR');
Quasi1=E1./sum(E1); %Normalise

Extinct_Theory1=1./(gamma.*Quasi1(1)); %Mean Time to Extinction (Theory)
Extinct_Theory1
```

```
b = triu(ones(N+2),1);
b=fliplr(b);
b(b==1) = [0;Quasi1];
b=b(1:N+1,1:N+1);
b(b==0)=NaN;
b(1)=0;
EigSoln=b;



EigSoln1=EigSoln;
EigSoln1(isnan(EigSoln1))=0;
EigSoln2=fliplr(EigSoln1);

for pp=0:N+1
    EigSum(pp+1)=sum(diag(EigSoln2,pp-1));
end
EigSum1=fliplr(EigSum);
%stairs(EigSum1) %Quasistationary for sum of I states

minusone=-ones(max(size(TempTruncated)),1);
TauEach=TempTruncated\minusone;

c = triu(ones(N+2),1);
c=fliplr(c);
c(c==1) = [0;TauEach];
c=c(1:N+1,1:N+1);
c(c==0)=NaN;
c(1)=0;
EigEachSoln=c;

hold on
plot([0:N],EigEachSoln(1,:),'--ob','markers',5)
DATA=importdata('B12.points');
DATA0=DATA(2:end);
DATA1=reshape(DATA0,[4,4501]);
```

```
j=1;
for i=1:size(DATA1,2)
    if DATA1(2,i)==0
        DATA4(j,1)=DATA1(1,i);
        DATA4(j,2)=DATA1(3,i);
       j=j+1;
    end
end



DATA5=sort(DATA4);
plot(DATA5(:,1),DATA5(:,2),'-.r');

ylabel('Expected Time to Extinction','FontSize',16);
xlabel('Initial Infectives','FontSize',16);
ylim([0,8.5]);
a_Leg=legend('Diffusion (Simulation)','Markov Chain','Finite Element','Fontsize',16,'
    Location','southeast');
set(a_Leg,'FontSize',16);

saveas(a_Fig,'k2_N20_B12.fig')
print('k2_N20_B12','-dpng')
```

7.2.5 Comparison of Andersson and Britton's approximation formula for time to extinction with simulation

Code as used in figure (28).

```
tic;
%Simulation of SEIR model for assorted values of N
%Outputs and saves percentage of extinctions by time (1/mu) expected life
%length

%stages
i=1;
j=1;
k=1;
```

```
SimNum=1000; %number of simulations

%parameters
N=100000;
epsilon=0.0003;
%R=15;
gamma=1/75;
r=1;
mu=gamma*epsilon;
Tmax=(2/mu);
for Rrange=1:16
    finish=tic;
    R=Rrange+4;
beta=gamma*R;

Outcome=zeros(1,11); %preallocating

p=i/(i+R-1);
xhat=1/R;
uhat=epsilon*(r)*((R-1)/R);
yhat=epsilon*((R-1)/R);

xhatvec=zeros(1,i);
for a=1:i
    xhatvec(1,a)=(p^(a-1))*((1-p)/(1-(p^i)))*(1/R);
end

uhatvec=zeros(1,j);
for a=1:j
uhatvec(1,a)=uhat/j;
end

yhatvec=zeros(1,k);
for a=1:k
yhatvec(1,a)=yhat/k;
end
```

```
Perc=zeros(SimNum,1);

%Consequence matrix
conseq=zeros(i+j+k,(2*i)+j+k+1);
conseq(1,1)=1;
for m=1:(i-1)
    conseq(m,m+1)=-1;
    conseq(m+1,m+1)=1;
end
conseq(i,i+1)=-1;
for m=1:i
conseq(m,i+1+m)=-1;
conseq(i+1,i+1+m)=1;
end
for m=1:(j-1)
    conseq(i+m,1+(2*i)+m)=-1;
    conseq(i+1+m,1+(2*i)+m)=1;
end
conseq(i+j,(2*i)+j+1)=-1;
conseq(i+j+1,(2*i)+j+1)=1;
for m=1:(k-1)
    conseq(i+j+m,1+(2*i)+j+m)=-1;
    conseq(i+j+m+1,1+(2*i)+j+m)=1;
end;
conseq(i+j+k,(2*i)+j+k+1)=-1;

InitialCond=round(N*[xhatvec uhatvec yhatvec]);


    %Simulations

parfor cc=1:SimNum

stsp=InitialCond;

%Start state
```

```
t=0;
T=0;



while  sum(stsp(1,(i+1):(i+j+k)))>0 && T < Tmax %Stops when no infected

%transition rates
a=mu*N;
b=zeros(i-1,1);
for m=1:(i-1)
b(m)=i*mu*stsp(1,m);
end
c=i*mu*stsp(1,i);
d=zeros(i,1);
for m=1:i
d(m)=(beta/N)*stsp(1,m)*sum(stsp(1,(i+j+1):(i+j+k)));
end
e=zeros(j-1,1);
for m=1:(j-1)
e(m)=j*(gamma/r)*stsp(1,i+m);
end
f=j*(gamma/r)*stsp(1,i+j);
g=zeros(k-1,1);
for m=1:(k-1)
g(m)=k*gamma*stsp(1,i+j+m);
end
h=k*gamma*stsp(1,i+j+k);

rate=a+sum(b)+c+sum(d)+sum(e)+f+sum(g)+h;

%cumulative sum matrix
summat=zeros(1,(2*i)+j+k+1);
summat(1,1)=a;
for m=1:(i-1)
summat(1,1+m)=a+sum(b(1:m));
end
```

```
summat(1,i+1)=a+sum(b)+c;
for m=1:i
summat(1,i+1+m)=a+sum(b)+c+sum(d(1:m));
end
for m=1:(j-1)
    summat(1,1+(2*i)+m)=a+sum(b)+c+sum(d)+sum(e(1:m));
end
summat(1,(2*i)+j+1)=a+sum(b)+c+sum(d)+sum(e)+f;
for m=1:(k-1)
    summat(1,1+(2*i)+j+m)=a+sum(b)+c+sum(d)+sum(e)+f+sum(g(1:m));
end;
summat(1,(2*i)+j+k+1)=a+sum(b)+c+sum(d)+sum(e)+f+sum(g)+h;

time=random('Exponential',1/rate); %decide when next step

   U=rand*rate;
   V=find(summat>U, 1 );
   W=transpose(conseq(:,V));
   stsp=stsp+W; %decide which next step




t=t+1;
W=T;
T=T+time;
end
toc(finish)
EX(cc,Rrange)=T;
end
end



toc
save('CCSResult')
```

7.2.6 Exploration of Critical Community Size as parameters vary, including Andersson and Britton's approximation

Code as used in figure (30).

```
tic;
%Simulation of SEIR model for assorted values of N
%Outputs and saves percentage of extinctions by time (1/mu) expected life
%length

%stages
i=1;
j=1;
k=1;



SimNum=1000; %number of simulations

%parameters
N=100000;
epsilon=0.0003;
%R=15;
gamma=1/75;
r=1;
mu=gamma*epsilon;
Tmax=(2/mu);
for Rrange=1:16
    finish=tic;
    R=Rrange+4;
beta=gamma*R;

Outcome=zeros(1,11); %preallocating

p=i/(i+R-1);
xhat=1/R;
uhat=epsilon*(r)*((R-1)/R);
yhat=epsilon*((R-1)/R);
```

```
xhatvec=zeros(1,i);
for a=1:i
    xhatvec(1,a)=(p^(a-1))*((1-p)/(1-(p^i)))*(1/R);
end

uhatvec=zeros(1,j);
for a=1:j
uhatvec(1,a)=uhat/j;
end

yhatvec=zeros(1,k);
for a=1:k
yhatvec(1,a)=yhat/k;
end

Perc=zeros(SimNum,1);

%Consequence matrix
conseq=zeros(i+j+k,(2*i)+j+k+1);
conseq(1,1)=1;
for m=1:(i-1)
    conseq(m,m+1)=-1;
    conseq(m+1,m+1)=1;
end
conseq(i,i+1)=-1;
for m=1:i
conseq(m,i+1+m)=-1;
conseq(i+1,i+1+m)=1;
end
for m=1:(j-1)
    conseq(i+m,1+(2*i)+m)=-1;
    conseq(i+1+m,1+(2*i)+m)=1;
end
conseq(i+j,(2*i)+j+1)=-1;
conseq(i+j+1,(2*i)+j+1)=1;
for m=1:(k-1)
    conseq(i+j+m,1+(2*i)+j+m)=-1;
```

```
    conseq(i+j+m+1,1+(2*i)+j+m)=1;
end;
conseq(i+j+k,(2*i)+j+k+1)=-1;

InitialCond=round(N*[xhatvec uhatvec yhatvec]);


    %Simulations

parfor cc=1:SimNum

stsp=InitialCond;

%Start state
t=0;
T=0;



while  sum(stsp(1,(i+1):(i+j+k)))>0 && T < Tmax %Stops when no infected

%transition rates
a=mu*N;
b=zeros(i-1,1);
for m=1:(i-1)
b(m)=i*mu*stsp(1,m);
end
c=i*mu*stsp(1,i);
d=zeros(i,1);
for m=1:i
d(m)=(beta/N)*stsp(1,m)*sum(stsp(1,(i+j+1):(i+j+k)));
end
e=zeros(j-1,1);
for m=1:(j-1)
e(m)=j*(gamma/r)*stsp(1,i+m);
end
f=j*(gamma/r)*stsp(1,i+j);
```

```
g=zeros(k-1,1);
for m=1:(k-1)
g(m)=k*gamma*stsp(1,i+j+m);
end
h=k*gamma*stsp(1,i+j+k);

rate=a+sum(b)+c+sum(d)+sum(e)+f+sum(g)+h;

%cumulative sum matrix
summat=zeros(1,(2*i)+j+k+1);
summat(1,1)=a;
for m=1:(i-1)
summat(1,1+m)=a+sum(b(1:m));
end
summat(1,i+1)=a+sum(b)+c;
for m=1:i
summat(1,i+1+m)=a+sum(b)+c+sum(d(1:m));
end
for m=1:(j-1)
    summat(1,1+(2*i)+m)=a+sum(b)+c+sum(d)+sum(e(1:m));
end
summat(1,(2*i)+j+1)=a+sum(b)+c+sum(d)+sum(e)+f;
for m=1:(k-1)
    summat(1,1+(2*i)+j+m)=a+sum(b)+c+sum(d)+sum(e)+f+sum(g(1:m));
end;
summat(1,(2*i)+j+k+1)=a+sum(b)+c+sum(d)+sum(e)+f+sum(g)+h;

time=random('Exponential',1/rate); %decide when next step

   U=rand*rate;
   V=find(summat>U, 1 );
   W=transpose(conseq(:,V));
   stsp=stsp+W; %decide which next step



t=t+1;
```

```
W=T;
T=T+time;
end
toc(finish)
EX(cc,Rrange)=T;
end
end


toc
save('CCSResult')
```

7.2.7 Comparison of approximation and simulation of ρ

Code as used in figure (31).

```
clear all
tic;
N=100000;
r=0.5;
mu=1/70;
R=15;
gamma=52;
beta=780;
epsilon=mu/gamma;

Tmax=4;

i=11;
j=4;
k=4;
ooo=100; %iterations

p=i/(i+R-1);

xhat=1/R;
uhat=epsilon*(r)*((R-1)/R);
yhat=epsilon*((R-1)/R);
```

```
xhatvec=zeros(1,i);
for a=1:i
    xhatvec(1,a)=(p^(a-1))*((1-p)/(1-(p^i)))*(1/R);
end

uhatvec=zeros(1,j);
for a=1:j
uhatvec(1,a)=uhat/j;
end

yhatvec=zeros(1,k);
for a=1:k
yhatvec(1,a)=yhat/k;
end

%Consequence matrix
conseq=zeros(i+j+k,(2*i)+j+k+1);
conseq(1,1)=1;
for m=1:(i-1)
    conseq(m,m+1)=-1;
    conseq(m+1,m+1)=1;
end
conseq(i,i+1)=-1;
for m=1:i
conseq(m,i+1+m)=-1;
conseq(i+1,i+1+m)=1;
end
for m=1:(j-1)
    conseq(i+m,1+(2*i)+m)=-1;
    conseq(i+1+m,1+(2*i)+m)=1;
end
conseq(i+j,(2*i)+j+1)=-1;
conseq(i+j+1,(2*i)+j+1)=1;
for m=1:(k-1)
    conseq(i+j+m,1+(2*i)+j+m)=-1;
    conseq(i+j+m+1,1+(2*i)+j+m)=1;
```

```
end;
conseq(i+j+k,(2*i)+j+k+1)=-1;

%Simulation of SEIR model

parfor ppp=1:ooo
%Initial Conditions
InitialCond=round(N*[xhatvec uhatvec yhatvec]);
stsp=InitialCond;
t=0;
T=0;
W=0;
conseq;

while  sum(stsp(1,(i+1):(i+j+k)))>0 && T < Tmax %Stops when no infected

%transition rates
a=mu*N;
b=zeros(i-1,1);
for m=1:(i-1)
b(m)=i*mu*stsp(1,m);
end
c=i*mu*stsp(1,i);
d=zeros(i,1);
for m=1:i
d(m)=(beta/N)*stsp(1,m)*sum(stsp(1,(i+j+1):(i+j+k)));
end
e=zeros(j-1,1);
for m=1:(j-1)
e(m)=j*(gamma/r)*stsp(1,i+m);
end
f=j*(gamma/r)*stsp(1,i+j);
g=zeros(k-1,1);
for m=1:(k-1)
g(m)=k*gamma*stsp(1,i+j+m);
end
h=k*gamma*stsp(1,i+j+k);
```

```
rate=a+sum(b)+c+sum(d)+sum(e)+f+sum(g)+h;

%cumulative sum matrix
summat=zeros(1,(2*i)+j+k+1);
summat(1,1)=a;
for m=1:(i-1)
summat(1,1+m)=a+sum(b(1:m));
end
summat(1,i+1)=a+sum(b)+c;
for m=1:i
summat(1,i+1+m)=a+sum(b)+c+sum(d(1:m));
end
for m=1:(j-1)
    summat(1,1+(2*i)+m)=a+sum(b)+c+sum(d)+sum(e(1:m));
end
summat(1,(2*i)+j+1)=a+sum(b)+c+sum(d)+sum(e)+f;
for m=1:(k-1)
    summat(1,1+(2*i)+j+m)=a+sum(b)+c+sum(d)+sum(e)+f+sum(g(1:m));
end;
summat(1,(2*i)+j+k+1)=a+sum(b)+c+sum(d)+sum(e)+f+sum(g)+h;

time=random('Exponential',1/rate); %decide when next step

   U=rand*rate;
   V=find(summat>U, 1 );
   W=transpose(conseq(:,V));
   stsp=stsp+W; %decide which next step


t=t+1;
T=T+time;
end
Tempmat=stsp-W;
Tempmat1=stsp;

TempTempmat(:,ppp)=[Tempmat];
```

```
Varmat1(:,ppp)=[sum(Tempmat(:,1:i),2) sum(Tempmat(:,(i+1):(i+j)),2) sum(Tempmat(:,(i+j+1)
    :(i+j+k)),2)];
Checkmat(:,ppp)=[sum(Tempmat1(:,1:i),2) sum(Tempmat1(:,(i+1):(i+j)),2) sum(Tempmat1(:,(i+
    j+1):(i+j+k)),2)];

jjmat(:,ppp)=Tempmat(i+j)/(sum(Tempmat(:,(i+1):(i+j)),2));

end
hist(jjmat,20)
nanmean(jjmat)
```

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